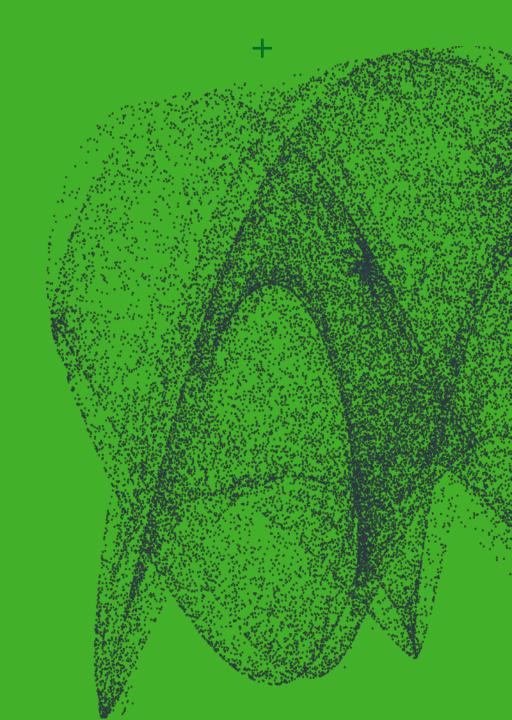


Drug Expenditure Dynamics 1995-2020

Understanding Medicine Spending in Context Country Detail Appendix:

Spain



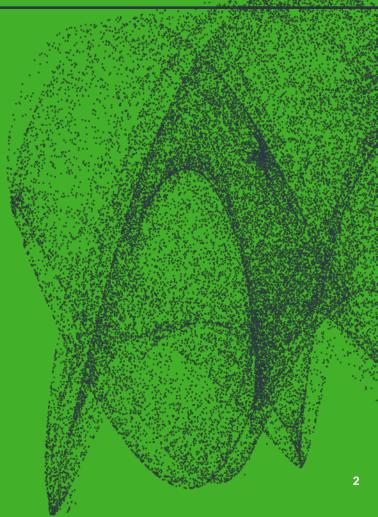
Introduction

- This document is intended as an accompanying appendix to the report Understanding the Dynamics of Drug Expenditure 1995-2020.
- The report includes analyses of 11 major countries and provides cross-country and aggregate analyses of these markets.
- This document includes specific country analyses mirroring the main report and intended to illustrate the same dynamics in each country that are shown across countries.
- In some cases, there are important differences from cross-country trends and those are illustrated and highlighted.
- The key findings in relation to each country are summarized and each page represents a specific analysis of interest.
- This document is not an exhaustive analysis or summary of the country, and the primary purpose is to provide the long-history analyses which are unique to this report.
- The exhibits in this report are sometimes complex or include multiple graphics per page. This document ends with several annotated examples of the layout of important exhibits to enable the reader to better understand how to read and understand them.





Spain

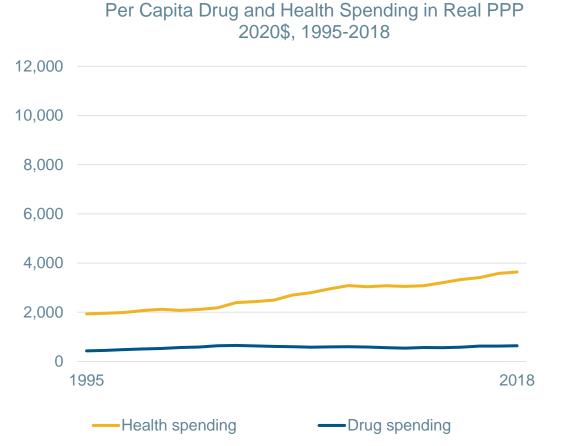


Key findings

- Spain drug spending is 18% of healthcare spending in 2018 but has been declining for many years and may represent a higher share due to lower overall healthcare costs than other comparison countries.
- Drug spending includes retail pharmacy drugs, which represent 15% of total healthcare spending with an additional 3% of healthcare spending from non-retail, with retail down from higher levels in the early 2000s.
- Spending has been distributed between brands and generics in relatively unchanged patterns for the past 10 years, despite significant increases in protected brand spending as generic volume itself continues to increase.
- The therapy area focus of spending has shifted from traditional classes which dominated in 2000 to more specialty classes in 2020. Overall, the top five classes of 1995 (antithrombotics, anti-diabetics, mental health, anti-bacterials, and cardiovascular) represented about 41% of drug spending in 2000, but only 22% of spending in 2020, predominantly driven by genericization. The current leading classes (oncologics, immunology, anti-diabetics, cardiovascular, and neurology) were 45% of spending in 2020, rising from 25% in 2000, illustrating a shift due to the influx of new treatment options.
- Some classes (i.e., cholesterol, anti-ulcerants) have had important innovation peaking in the early 2000s, with a continuous genericization resulting in dramatic declines in the cost of those medicines.
- Other classes (i.e., immunology, oncology) had continuous introduction of new innovative drugs which were either added to regimens or supersede previous standards of care, but which are still to be offset by upcoming LOE in the next five years.
- Some classes (e.g., antithrombotics) have experienced a mix of these patterns, where a group of medicines have been widely adopted, ultimately lose exclusivity and become less costly, later to be superseded by a new medicine type.
- Viral hepatitis spending peaked in 2015 at 13% of drug spending at list prices, but significant discounts were negotiated between industry and the government and total net drug spending only increased by less than 1% of health spending.

Spain drug spending is 18% of healthcare spending in 2018, but has been declining for many years

Drug and Healthcare Spending 1995-2018



Drug Share of Healthcare Spending in Real PPP 2020\$.1995-2018

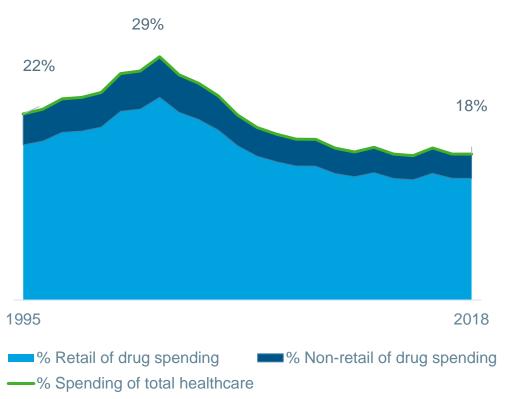
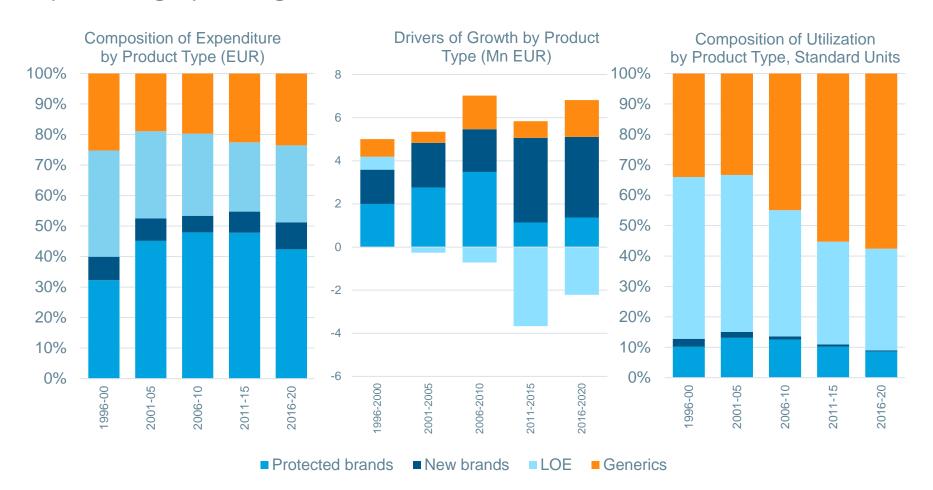


Chart notes: See Methodology for details.

Source: World Health Organization (WHO), 2018 (extracted on 18 Aug 2021); WHO SHE 1.0 data (extracted on 18 Aug 2021); OECD, 2019 (extracted on 18 Aug 2021); IQVIA Institute, Sep 2021

Growth by new brands continues as the cycle of genericization results in lower costs in those medicines

Spain Drug Spending and Utilization 1995-2020

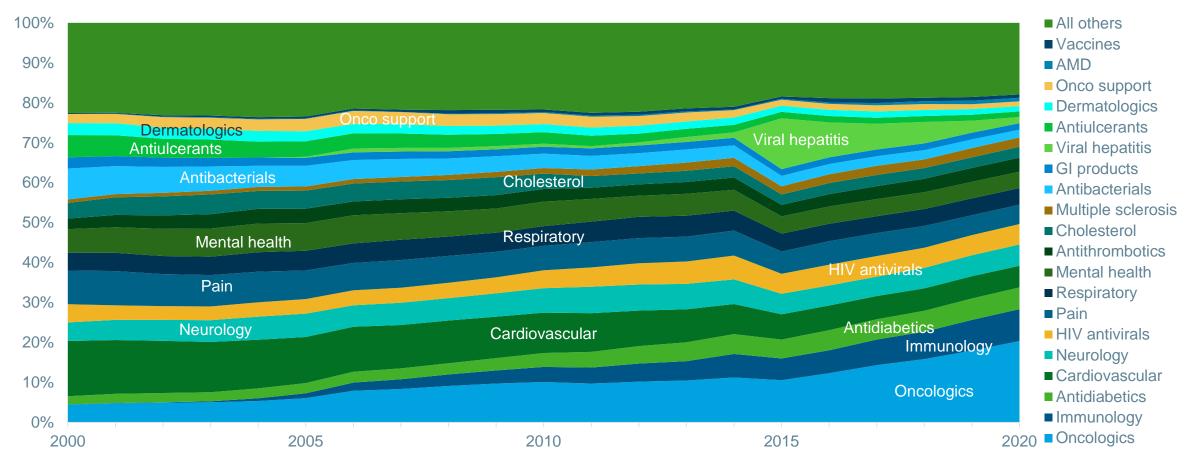


- Protected brands have a decreasing share of spending, offset by new brand spending in the past decade consistent with shifts in national pricing policy
- Most growth is driven by new brands, including protected products, and offset by losses of exclusivity
- Generic segments increasing is also consistent with shifts in policy



Spending has shifted from older traditional drugs to a greater focus on specialty therapies in recent years

Spain Composition of Drug Real Local Currency Spending by Drug Class, 2000-2020

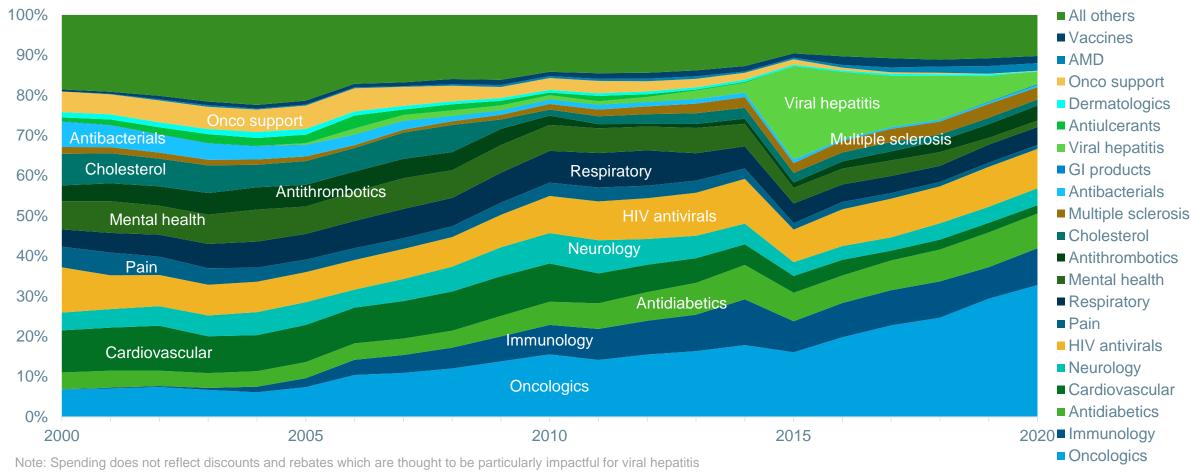


Note: Spending does not reflect discounts and rebates which are thought to be particularly impactful for viral hepatitis Source: IQVIA MIDAS; IQVIA Institute, Dec 2020



Oncologics, immunology, anti-diabetics & HIV collectively increased spending share from 19% in 2000 to 42% in 2020

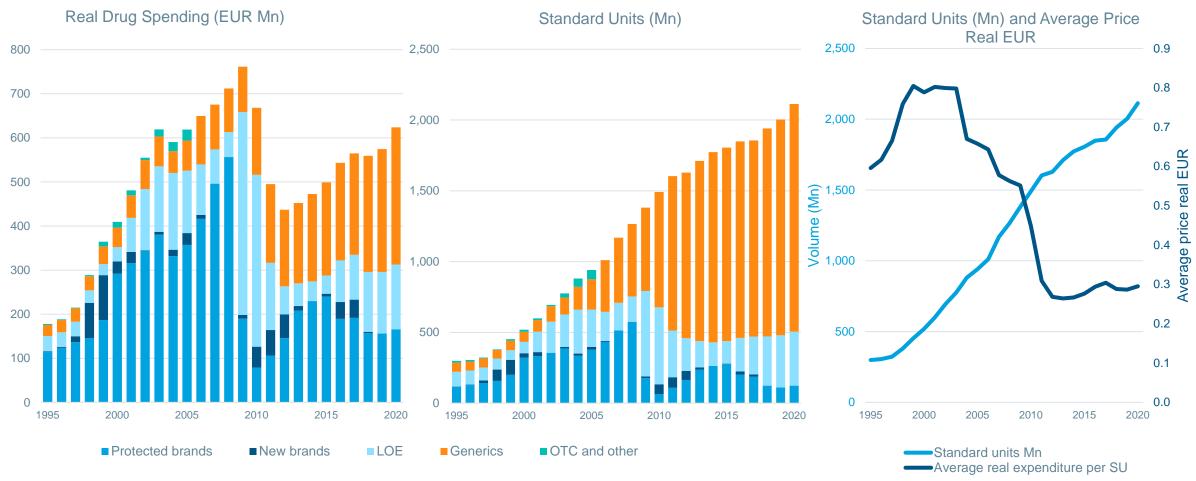
Spain Composition of Protected Brands Real Local Currency Spending by Drug Class, 2000-2020





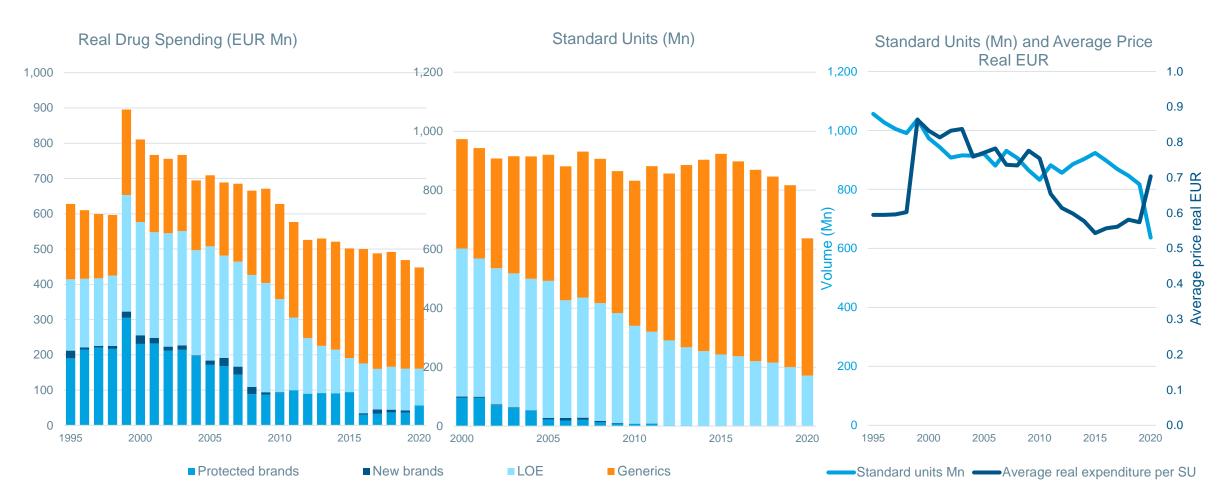
While volumes increased by 600% over 25 years, spending only increased by 250% as protected brands lost significant share

Spain Cholesterol Volumes, Average Prices and Spending by Product Type, 1995-2020



Anti-bacterials have been highly genericized while volume has been declining

Spain Anti-bacterial Volumes, Average Prices and Spending by Product Type 2000-2020



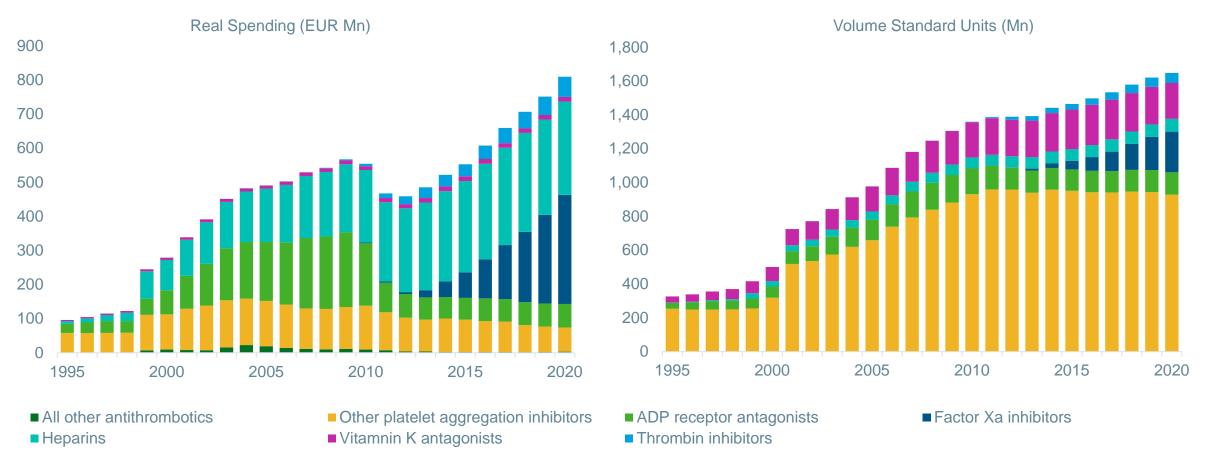
Anti-ulcerant spending has declined as costs have dropped and volume has been steady at a high level in the past decade

Spain Anti-Ulcerants Volumes, Average Prices and Spending by Product Type 1995-2020



Antithrombotic spending increased recently with uptake in Factor Xa inhibitors

Spain Antithrombotics Spending and Volumes by Drug Type, 1995-2020



Note: Heavily non-retail therapies in this class are understated in 1995-1998 as the hospital audit was added in 1999



Hypertension usage reflects addition of newer mechanisms to treatment regimens even as spending has slowed due to expiries

Spain Hypertension Spending and Volume by Mechanism, 1995-2020

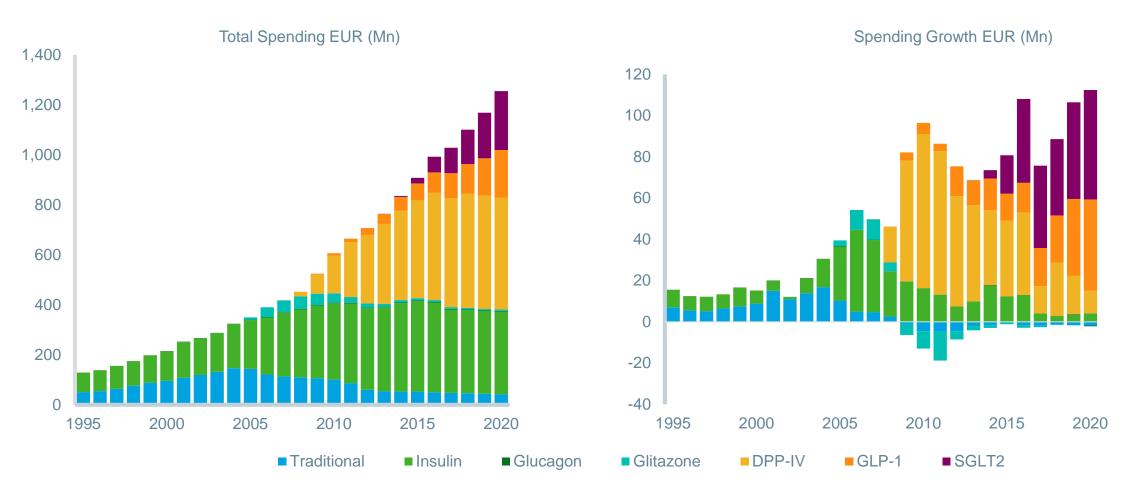


Chart notes: ARBs: Angiotensin II receptor antagonists, CCBs: Calcium channel blockers; ACEs: Angiotensin-converting enzyme. Source: IQVIA MIDAS; IQVIA Institute, Dec 2020



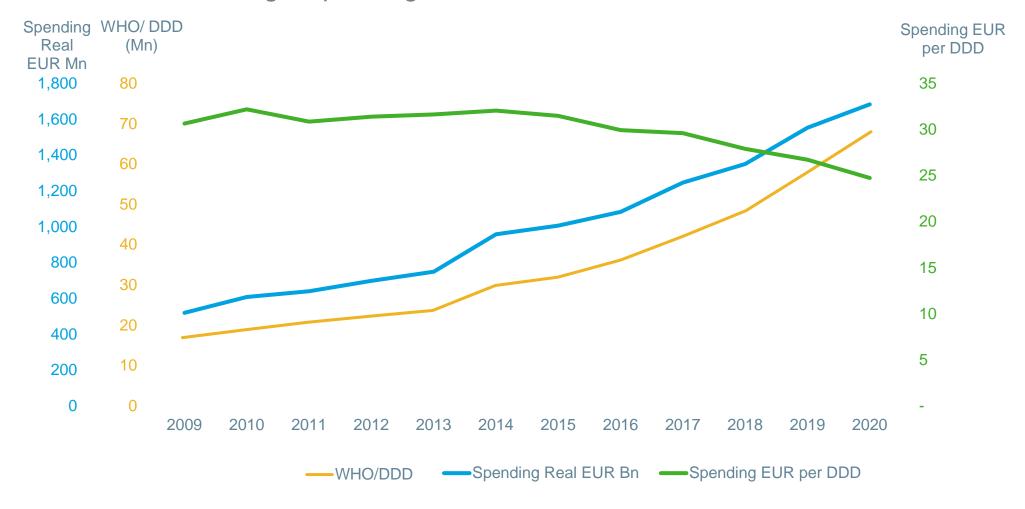
Novel diabetes drugs drive spending growth since 2008 while insulins and traditional remain steady

Spain Diabetes Real Spending and Growth EUR (Mn) by Drug Type, 1995-2020



Auto-immune usage nearly tripled over the past decade, while cost per day declined 19% in the last few years from biosimilars

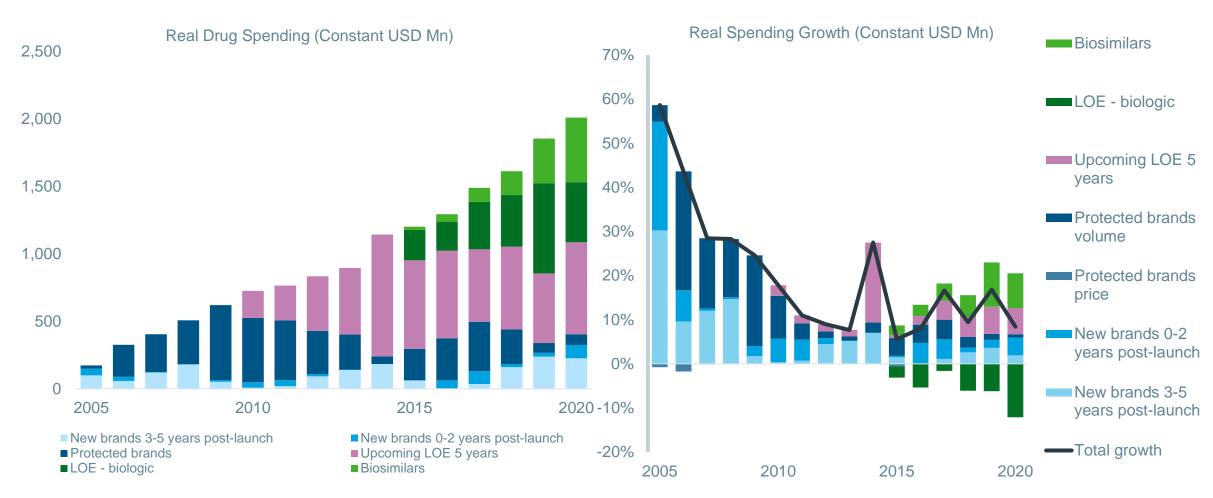
Spain Auto-immune Biologic Spending, DDD and Cost, 2009-2020





Auto-immune growth has slowed from biosimilars since 2015

Spain Autoimmune Biologic Invoice Spending and Growth Drivers, 2005-2020



Vaccine spending includes significant peaks for adoption of the meningitis, rotavirus, and pneumonia vaccines

Spain Vaccine Spending and Volumes by Drug Type, 2010-2020

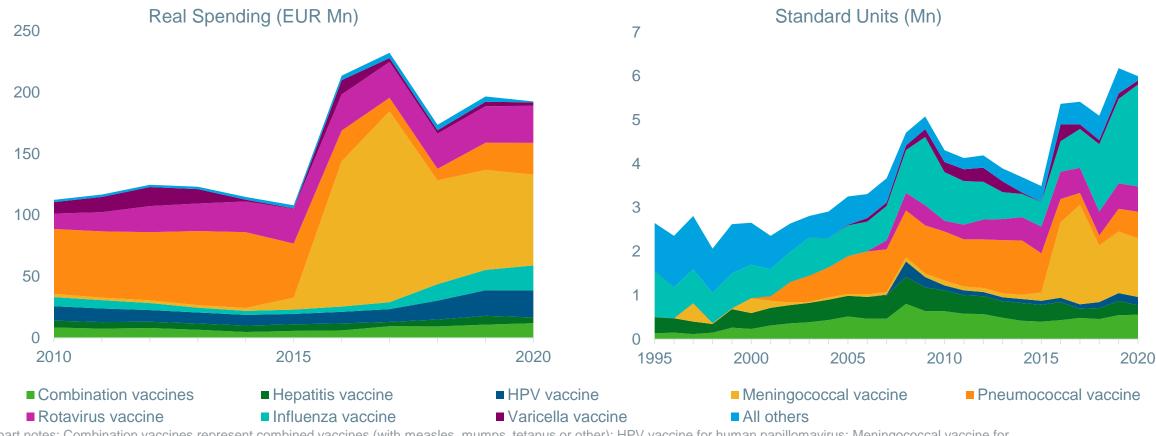
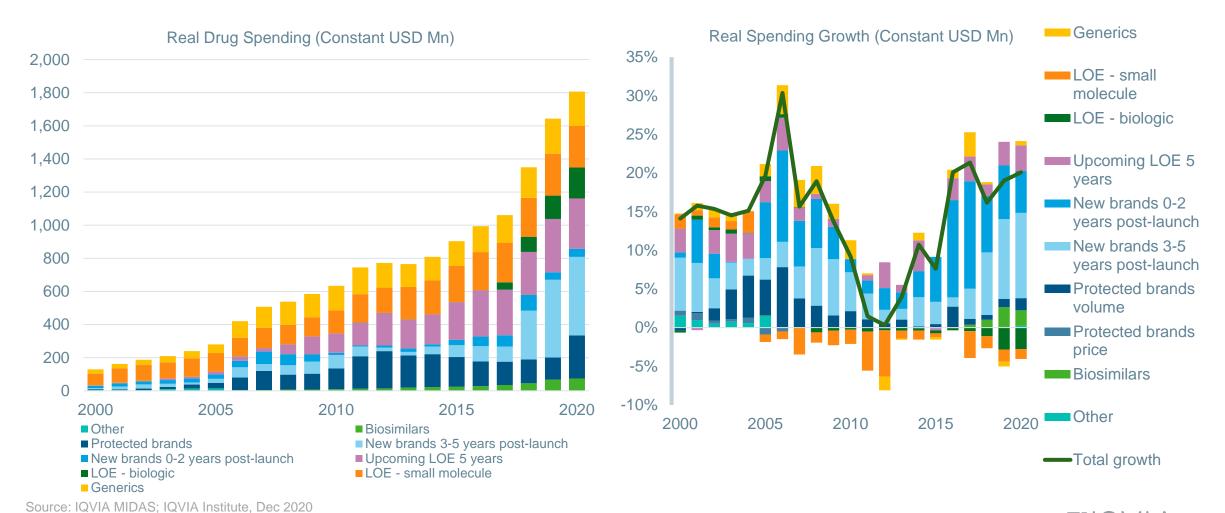


Chart notes: Combination vaccines represent combined vaccines (with measles, mumps, tetanus or other); HPV vaccine for human papillomavirus; Meningococcal vaccine for meningitis; Pneumococcal vaccine for pneumonia; Rotavirus vaccine for rotavirus; Influenza vaccine for the flu; Varicella vaccine for shingles; and All others for cholera, tetanus, typhoid and other viral/bacterial vaccines



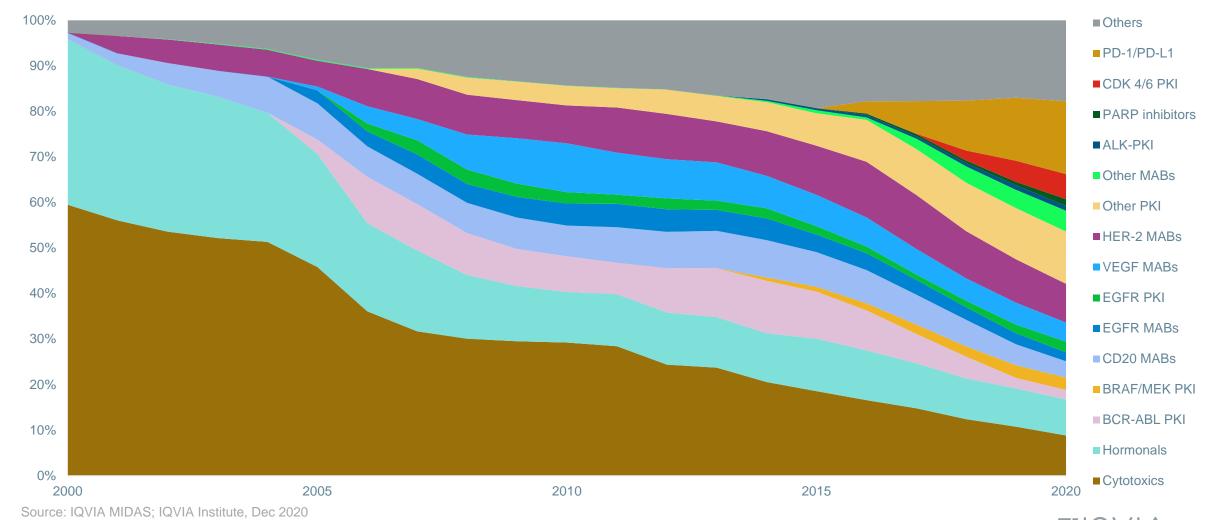
Oncology growth has been driven by newer drugs and offset modestly by biosimilars and generics

Spain Oncology Invoice Spending and Spending Growth Drivers, 2000-2020



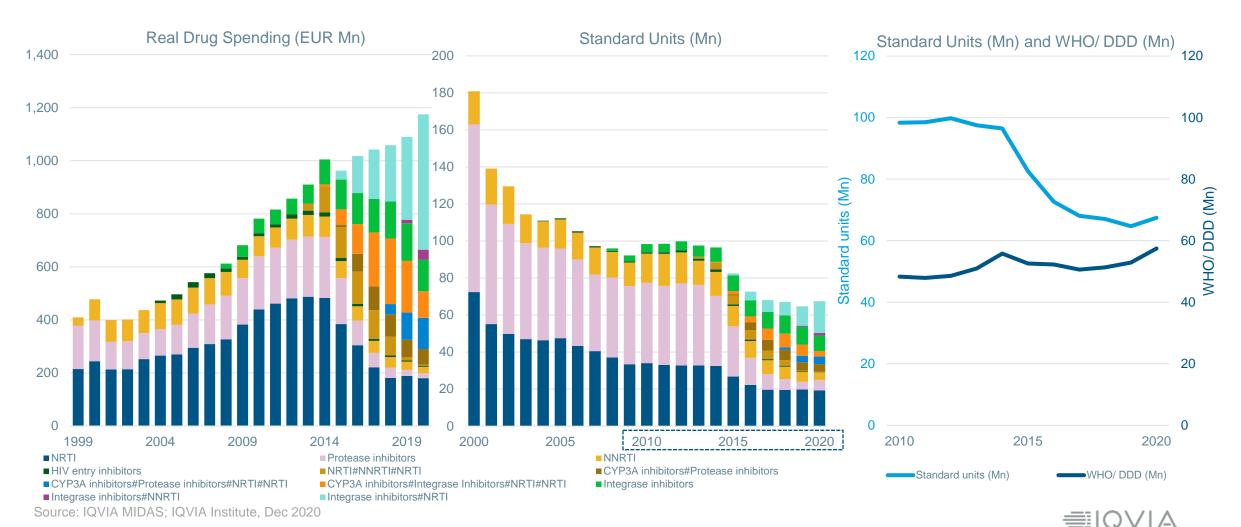
Oncology spending reflects strong uptake of newer mechanisms including PD-1/PD-L1, CDK 4/6 and many other biomarker targets

Spain Oncology Real Local Currency Spending by Mechanism, 2000-2020



In the last five years, HIV combination treatments gained higher spending than conventional NRTIs and protease inhibitors

Spain HIV Spending and Volume by Mechanism 2000-2020



Mental health growth is primarily volume driven as there has been relatively little innovation in recent years

Spain Mental Health Spending by Mechanism, Volume and Annual Growth by Product Type, 1995-2020

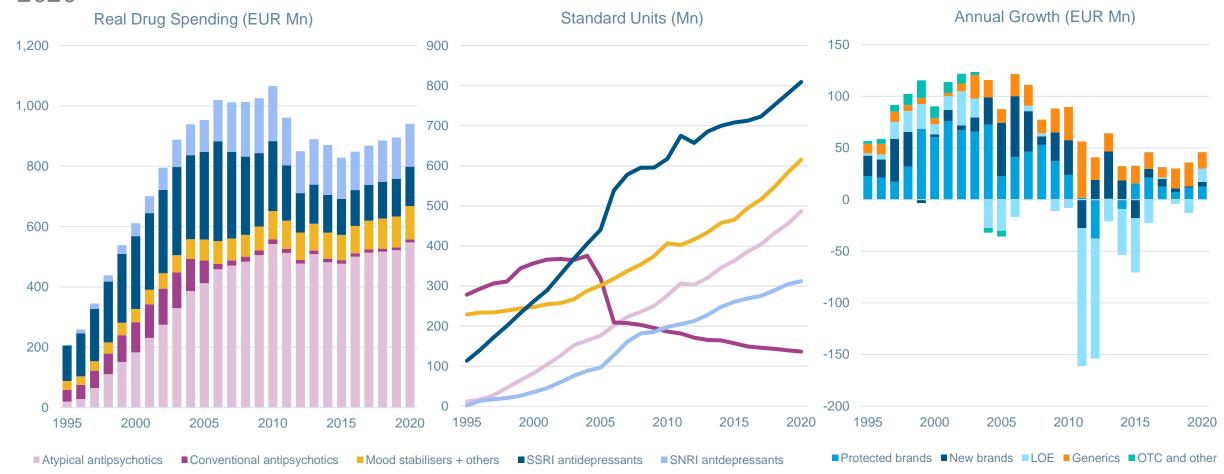
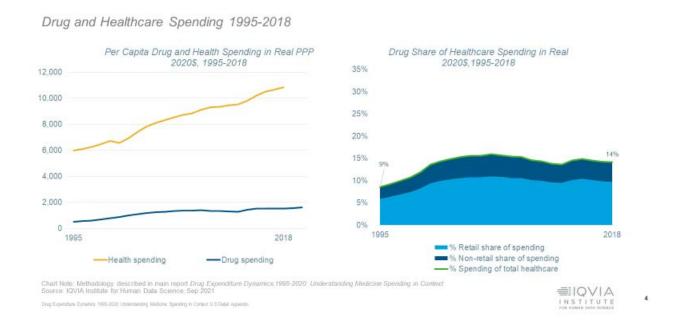




Illustration and explanation of data and chart layouts

Drug and Healthcare Spending Analyses

Key elements to note for interpreting charts



- Drug and healthcare spend have been adjusted for economic growth ('real' GDP growth has been removed), population growth, and for cost of living differences (Purchasing Power Parity – PPP).
- Drug spending as a percentage of healthcare spending uses estimates of total drug spending in all channels (retail and hospital) and after discounts and rebates.
- The hospital drug spend adds 1-11 percentage points, depending on the country, to the retail drug share of healthcare that is most often reported by governments (OECD).
- The right-most chart illustrates how much of overall drug spending is attributable to non-retail spending, which is significant and varies over time.



Drug spending is segmented by type of product, changing over time for some products to enable more complex analyses

Illustrating the Drug Type Segmentation Used in the Report

Drug Expenditure Segmented by Type of Drug

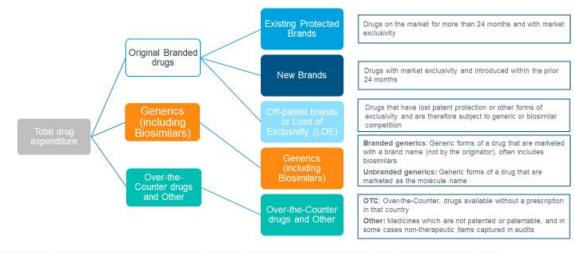


Chart notes: Protected brands include original protected brands, upcoming LOE and vaccines, New brands include original new brands; LOE include drugs that lost patent protection. Generics include non-original branded products as well as drugs that are marketed using the molecule name, OTC and other include non-prescription bound products and not patentable products. Due to the methods of combining multiple archived distabases, products which are no longer marketed but had spending or volume in 2005 or earlier are included in the other segment as specific segmentation was not possible.

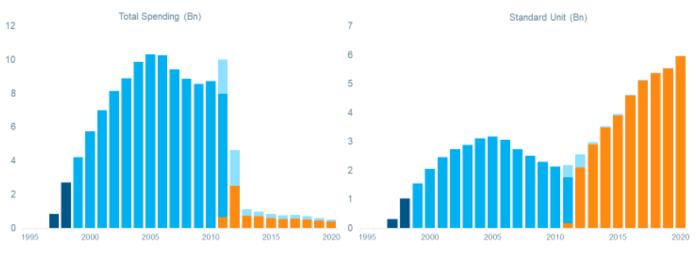
- Analyses in this report that use product segmentations as shown here are based on IQVIA audited data. They do not reflect payer net spending due to the confidential nature of some of the discounts and rebates. Unless a page indicates a non-IQVIA source, the analysis would not be adjusted for off-invoice discounts and rebates.
- Products have been segmented both by the way they are marketed (brands, generics, biosimilars, Over-the-counter) as well as by the status of their patent or other types of protection.
- Existing Protected brands are those which are no longer 'new' and are not yet offpatent.
- Nnew brands are defined as those products within their first 2 years in the market;
 however, some analytics in this report specifically identify older new brands from 3-5 years after launch.
- Loss of exclusivity is the status for branded products that are off-patent or no longer protected (but still had sales in the market) and these terms are used interchangeably in the report.
- Generics and biosimilars are treated in the same segment unless noted specifically on the chart.
- Over-the-counter status is a country-specific regulatory status and some drugs have both prescription-bound and OTC packs in the market.
- Other is a status where products either do not have typical brand or generic or
 protection statuses or where the product is no longer marketed and it was not
 possible to apply segmentation.

FOR HUMAN DATA SCIENCE

Illustration: product segmentation drug lifecycle dynamics

Example of Drug Type Segmentation using a single medicine

Exhibit x: Illustration of U.S. branded and generic segmentation, Lipitor and Atorvastatin generics



■GENERICS (atorvastatin) ■PROTECTED BRANDS (Lipitor until LOE) ■LOE - After Loss of Exclusivity (Lipitor) ■NEW BRANDS (Lipitor 0-2 years after launch)

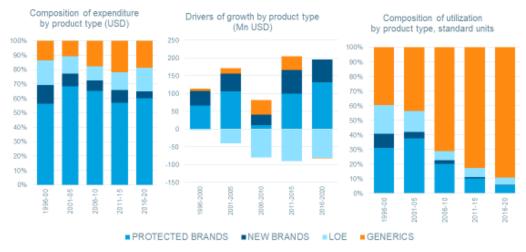
- In this example, the drug 'atorvastatin' begins life as a New Brand when Lipitor launched.
- The segmentation changes after 24 months to 'Protected Brand'. Analyses are based on quarterly time periods and a product may be considered new in 3 calendar years depending on the timing of launch in a country.
- At the point of patent expiry, the brand Lipitor becomes
 LOE, and new competing Generics enter the market.
- The left chart shows 'spending,' which is reflected in the currency noted on each chart. In the report the currencies. are most often normalized to real 2020\$ with constant US\$ exchange rates, but in the country appendix local currencies are used.
- The right chart shows values in standard units. Standard units vary by form and are generally not recommended to report in this aggregated way. However most drugs in the therapy areas were similar enough to enable this analysis.



Illustration of data and charts in this report

Country level overview of product types

Drug Spending and Utilization 1995-2020



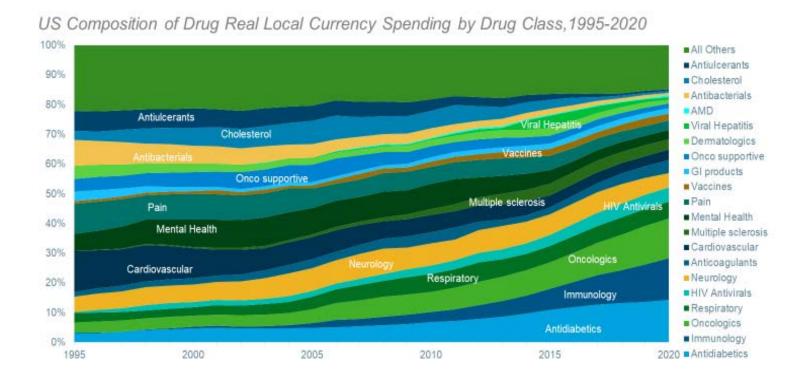
- Protected brands including new products average less than 70% of spending consistently
- Generic share of combined generic and LOE segments increasing steadily over time
- Generic share of volume increasing as generations of products shift to offpatent
- Most growth is driven by protected brands including new products, and offset by losses of exclusivity

- This analysis includes three views of drug spending, growth and volume in standard units, each present in the cross-country comparison section of the report and repeated in the beginning of each country section of the appendix.
- Spending is IQVIA audited sales and does not reflect off-invoice discounts and rebates.
- The drivers of growth chart is represented in absolute values of the currency noted.
- Products each have a segment status in each time period, and growth is a representation of the current group of products and their growth compared to prior periods. The product status in the prior period is not considered.
- Growth on an annual basis has been added together into 5-year groupings.
- Standard units are highly dissimilar by formulation and not recommended.



Illustration of data and charts in this report

Total drug spending over time on 100% scale by top 20 Therapy areas

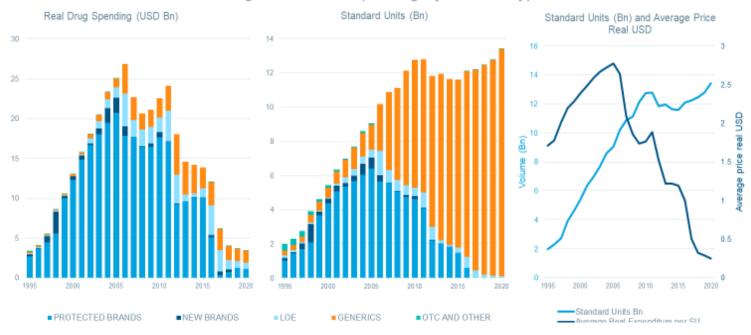


- Total IQVIA audited spending over 25 years has been collated and grouped by therapy areas.
- The therapy areas are defined by IQVIA with details of the definitions in the main report methodology section.
- The therapy areas called out by name are the classes that were ranked in the top 20 the most often across the eleven countries studied across the 25 years. This can mean that some classes which have declined in sales outside the top 20 in the most recent period are still shown.

Therapy area charts with sales, volume and cost by type of drug

Example of single therapy area with multiple metrics analyzed



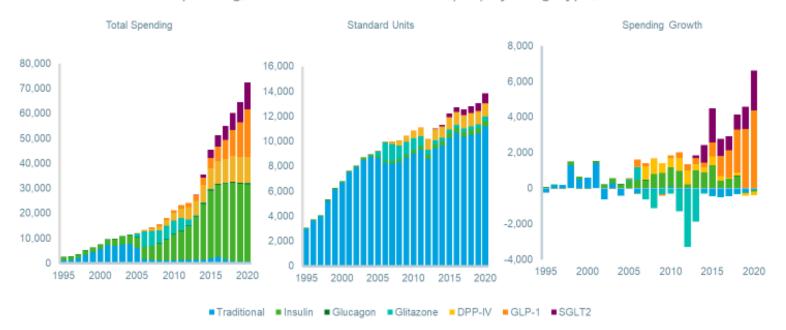


- Some analyses show three charts in this orientation, with spending, standard unit volume and finally a chart of volume and average cost per standard unit.
- Spending and cost are based on IQVIA audited data and do not reflect discounts and rebates.
- The segmentations shown in the charts are the same as described earlier.
- The average cost calculation is at the therapy area level.

Therapy areas showing subclasses by mechanism of action

Illustration of a therapy area using multiple analysis metrics





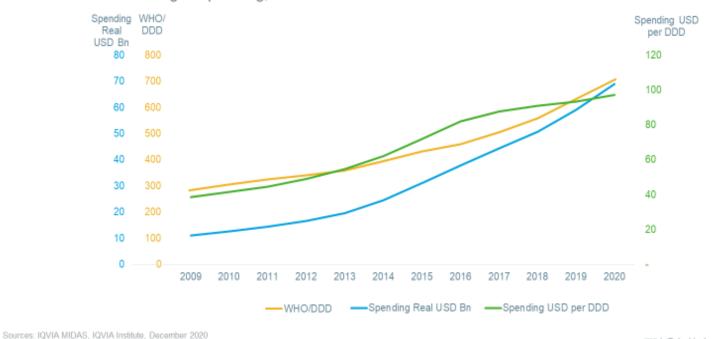
- Some therapy area charts include spending, standard units and spending growth.
- All are shown in the currency value noted.
- therapy sub segments, typically indicating shifts in the types of medicines used over time.

Autoimmune biologic charts

Illustration of three metrics on three axes on the same chart

Cost per day in immunology had been rising rapidly but has slowed since the first introduction of biosimilars in 2016

US Auto-immune Biologic Spending, DDD and Cost 2009-2020



- This chart layout is used for the autoimmune biologic market.
- It has 3 axes which are color-matched to the lines
- Two axes are on the left (sales and volume in WHO Defined Daily Doses – WHODDD). The color of the lines matches the color used on the axis to show increments.
- WHODDD represent a standardized dose used for all patients and normalized for packaging and formulation differences which are common with some products in this therapy area.
- WHODDD is particularly helpful for comparisons when original and biosimilar products are packaged differently from each other.

21



Charts using a more granular product type view

Illustration of product type segmentation with forward-looking segment

More than half of autoimmune biologic spending is due to lose exclusivity in next 5 years

U.S. Auto-immune Biologic Invoice Spending and Growth Drivers, 2005-2020



- Oncology and Autoimmune charts employ a more granular time-dependent segmentation of product type than other analyses in the report.
- Original biologics and small molecules when off-patent are identified separately as well as generics (small molecule) and biosimilars.
- The autoimmune charts are limited to biologic products and therefore exclude some small molecule products that could be relevant in some analyses such as JAK inhibitors.
- The upcoming LOE 5 years segment is composed of different products each year as their status changes, and refers to the expected entry of biosimilars in key products in future years.
- New products are shown with both 0-2 years and 3-5 year segments.
- Brands that are not 'new' and not LOE are shown as
 'protected' and growth charts are split by price and volume.

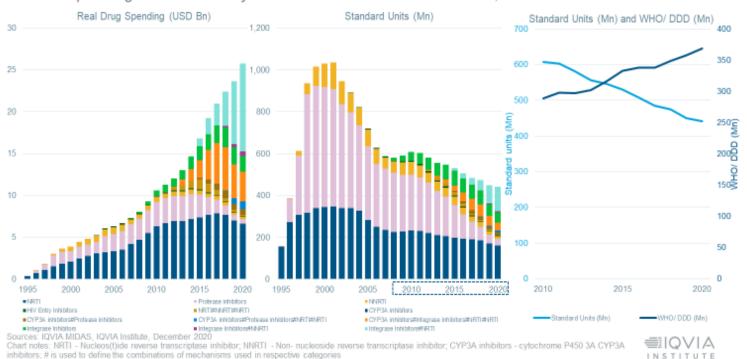


HIV market charts

Illustration of products with varying mechanisms of action

New combination treatments with low dosing regimens led to reduction in volume, offset by an increase of days of therapy

US HIV Spending and Volume by Mechanism 1995-2020 and DDD, 2010-2020



- Products in this market have been grouped by mechanism of action.
- Fixed-dose combination products are grouped by the type of mechanism of each ingredient, with each mechanism separated by a '#' symbol.
- Volume is measured in standard units in the middle chart.
- In the right chart, volume is in both standard units and WHO DDD, and the shift in the trajectory of these two measures suggests a changing number of doses per day as combination products become more common.



