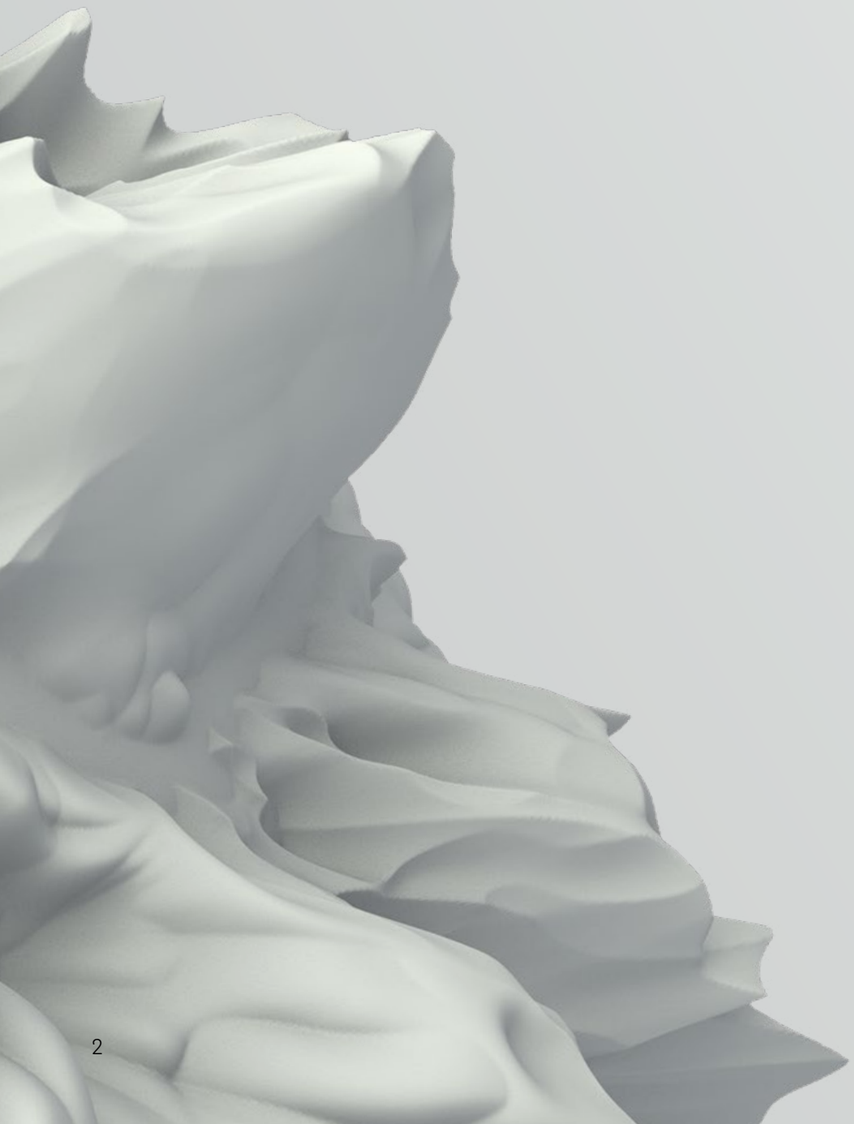
Clarivate™

# The future of the generics landscape 2021

Key branded drugs losing exclusivity in 2021 and beyond

# Loss of exclusivity for innovators means opportunity for imitators



## Patent expirations in specialty drugs and biologics offer potentially substantial cost savings to patients and payers

Generics comprise the majority of prescriptions in the world's top market places. Their share is only likely to grow, with biosimilars beginning to make a serious impact.

Generic drugs now account for 92% of all prescription drugs dispensed in the United States, according to figures from the International Generics and Biosimilar Medicines Association.[1] In Europe, 67% of drugs dispensed are generic, and in Japan, generics make up 77% of prescription drugs by volume.

**Generics broaden access to medicines and keep the engines of innovation going.** For the originators of drugs and biologics, loss of exclusivity is a last act in the cycle of innovation. Their monopoly window, in which they must recoup the costs of innovation and generate funding for future R&D, has closed. Their commercial efforts wind down, and they move on to newer drugs, while an ecosystem of generics companies advances to manufacture more affordable copies.

Originators can employ a variety of strategies to hold on to market share and recoup losses, including life cycle management, manufacturing their own branded generics or partnering with generics manufacturers on authorized generics, allowing them to recoup some of their losses. Nonetheless, for small molecule drugs, the decline in sales is typically steep. When atorvastatin (Lipitor), then the world's best-selling statin, lost exclusivity in 2012, global revenues dropped from 2011's $9.58 billion to $3.95 billion within 12 months.[2] However, Lipitor/atorvastatin was still generating revenues of $1.97 billion in 2019,[3] just before Pfizer offloaded the drug with the merger of Upjohn and Mylan — a shadow of its $12.89 billion peak in 2006,[4] but a blockbuster twice over nonetheless.

**Biosimilars ease cost burdens from older biologics, but face a tougher path to market.** Biologics are a somewhat different story, being much more difficult and expensive to develop and impossible to duplicate precisely. The process of developing a biosimilar incurs much of the risk and expense involved in developing the initial biologic, and the approvals process is accordingly far more rigorous. As such, biologics can enjoy years of effective monopoly even after loss of exclusivity and tend to retain more market share even after the entry of biosimilar competitors.[5] In addition, physicians are often reluctant to switch patients to a biosimilar, given that these therapeutics are not identical to the molecules they are designed to imitate — a 2019 survey of U.S. physicians by Clarivate found that 17% agreed that they were uncomfortable using biosimilars because of concerns about efficacy and the rigor of the approvals process (by contrast, 8% said their practices were encouraging prescriptions of biosimilars over their reference biologics).[6] Enbrel, which lost patent protection in Europe in 2014 and in the United States in 2016, saw its global revenues decline from $5.96 billion in 2016[7] to $5.22 billion in 2020.[8]

Roche has taken some of the biggest hits as biosimilars impacted its key biologics blockbusters. In 2014, the Swiss giant boasted three of the world's ten best-selling drugs, with Rituxan/Mabthera (5.6 billion Swiss francs, or CHF, in 2014 revenues), Avastin (6.4 billion CHF) and Herceptin (6.2 billion CHF) accounting for about a third of the company's revenues.[9] Between 2019 and 2020, revenues fell for each of the products, with Rituxan/Mabthera down to $4.22 billion, Avastin slipping to $4.99 billion and Herceptin declining to $3.73 billion.10

All eyes, however, will be on adalimumab (Humira), the world's best-selling drug, which sees its main U.S. patent expire in 2023. Already at least six biosimilar versions have been approved by the U.S. Food and Drug Administration (FDA), and given the size of the potential market — in 2020 Humira had global sales of $19.83 billion[11] — others can be expected to join the fray. In an attempt to fend off biosimilar competition when its European patents expired in October 2018, AbbVie introduced substantial discounting.[12] The company nonetheless saw Humira sales outside the United States slide 31% from 2018 to 2019, as biosimilar competitors entered the European market, and faces a slew of potential adalimumab competitors when it loses U.S. patent protection in 2023.[13]

**Benefits for patients and payers may vary.**

Conventional wisdom would suggest that patent expiries bring competition, leading to lower prices for patients, but in practice, cost savings can vary greatly across categories and markets.[14] Indeed, there is evidence that when the market is competitive, with a number of potential suppliers and rules in place to allow pharmacists to dispense generics even though a prescription has been written for a brand name version, generics can achieve high levels of market penetration, making treatments available to a much broader pool of patients.

However, fewer generic competitors can mean much lower cost savings to patients and payers.[15] Drug shortages can also contribute to continued high prices. Recent anti-trust litigation[16] alleges a variety of anticompetitive practices pursued by some generics manufacturers, which may have contributed to artificially high prices for some common generic drugs.

For the most part, though, genericization enables more patients to access newer medicines, alleviates cost pressures on payers and spurs manufacturers to further innovations, to the benefit of future generations of patients.

## Contents

# Methodology

## This report showcases generic drugs losing exclusivity in 2021 and beyond with the potential to impact the generics market.

**Data and analysis to identify the list drew from Clarivate Cortellis Generics Intelligence™, the world's only source of reliable and integrated market performance, manufacturing and patent data in a single, easily searchable solution, and Disease Landscape & Forecast™, which provides comprehensive market intelligence and actionable insights across 180+ indications to help optimize long-term disease strategies.**

Selection criteria:

- We selected molecules with a Constraint Date Forecast between 2021–2027 in key regions (United States, Europe [with focus on France, the United Kingdom, Germany, Spain and Italy], Japan) for analysis. The Constraint Date Forecast is a proprietary analytic in Cortellis Generics Intelligence that forecasts when a product is expected to lose exclusivity in more than 37 global markets.
- We included only single ingredients and excluded combination products.
- We then filtered the dataset according to total global or regional sales by molecule as well as by therapeutic area.

We evaluated each product considering factors such as global and regional sales, market share and trends, price evolution, generic activity, generic competitiveness and U.S. patent challenges.

From there, we profiled a selected list of brands losing exclusivity in the next few years:

- **BROVANA® (arformoterol tartrate)**
- **JANUVIA® (sitagliptin phosphate)**
- **HUMIRA® (adalimumab)**
- **VEMLIDY® (tenofovir alafenamide)**
- **XARELTO® (rivaroxaban)**
- **CALQUENCE® (acalabrutinib)**

Finally, we identified antineoplastics as a specific therapeutic area with several brands expected to lose exclusivity during 2021–2026.

The drug snapshots within this report draw from interviews with experts in the Cortellis research team; Clarivate Cortellis Generics Intelligence including market performance data sourced from IBM, IQVIA and Global Pricing Innovations; Clarivate drug, disease landscape and forecast reports; and other industry sources.

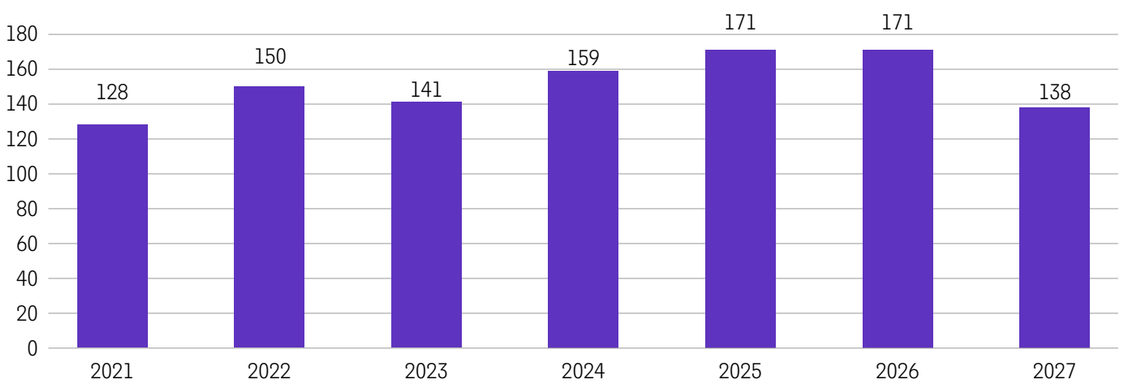
Please note that we generated the data shown in this report on April 14, 2021 and the data were correct as of that time.

# Loss of exclusivity overview
2021–2027

## Global

Over the next seven years, there are at least 120 molecules that are predicted to lose exclusivity annually in key global markets. These all have the potential to be genericized and contribute to more affordable health care for patients globally.

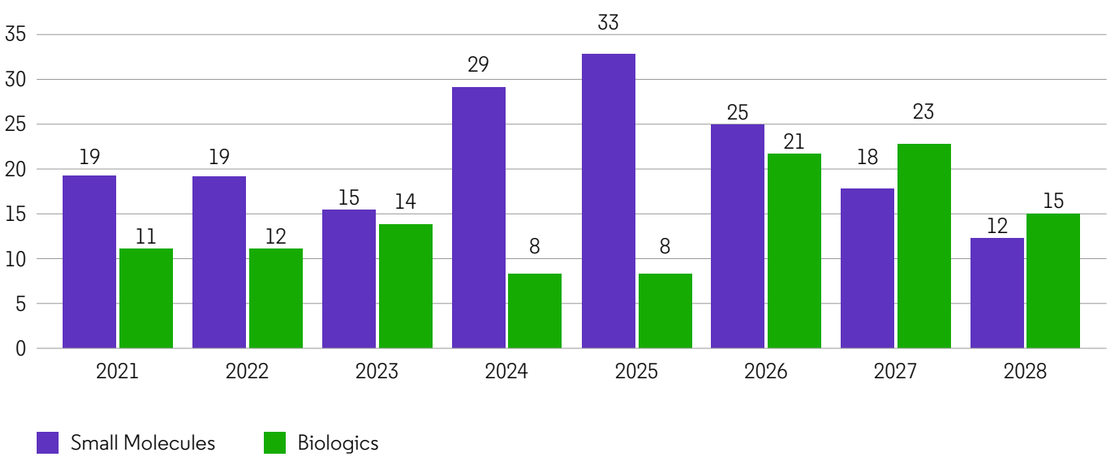
**Global loss of exclusivity landscape from 2021–2027**




## United States

There are numerous small molecule and biologic products that will have expiring patents and exclusivity in the United States, particularly for biologics between 2026 and 2028.

**U.S. loss of exclusivity landscape from 2021–2028**



# Loss of exclusivity overview
2021–2022

## Key markets

Although there are a number of products losing exclusivity in 2021, many countries will see a sharp increase in 2022. An ability to forecast which drugs will be impacted helps pharma companies plan accordingly and highlights opportunities for manufacturers.

## Top three brands losing exclusivity in each market in 2021

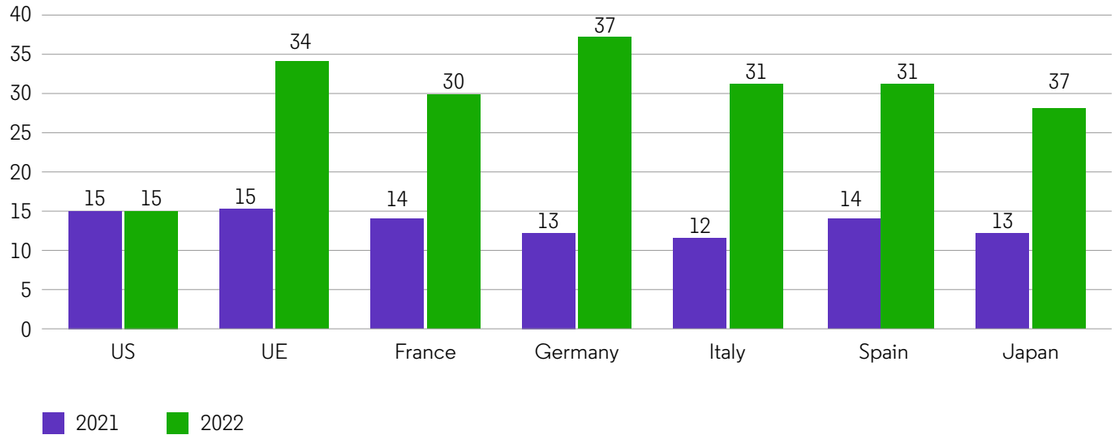
The top three brands that are expected to lose exclusivity in 2021 in each market according to global sales reported in Cortellis Generics Intelligence by molecule (Jan 1, 2020 to Dec 31, 2020):

**United States**
- BROVANA® $456 million
- JUBLIA® $453 million
- VOTRIENT® $567 million

**Europe (top five countries)**
- CIMZIA® $2.5 billion
- ESBRIET® $1.3 billion
- NEXAVAR® $0.5 billion

**Japan**
- VEMLIDY® $20.0 billion
- ALLERMIST® $6.4 billion
- XEPLION® $4.1 billion

**Global loss of exclusivity landscape by country in 2021–2022**



# Brovana

**What to watch: Will the declining market size discourage those with tentative approvals from launching, or will we see price erosion with multiple generics entering the market in 2021?**

**About BROVANA®**

- Marketed by Sunovion Pharmaceuticals Inc., a U.S. subsidiary of Sumitomo Dainippon Pharma Co., Ltd.

- Long-acting beta 2 adrenergic agonist (LABA) with bronchodilator activity used for symptomatic control of chronic obstructive pulmonary disease (COPD)

**BROVANA®**
**(arformoterol tartrate)**
Respiratory – chronic obstructive pulmonary disease

**2006**

First U.S. approval date:
October 6, 2006

**2021**

Numerous patent expiries:
June 22 – November 9, 2021
(U.S.)

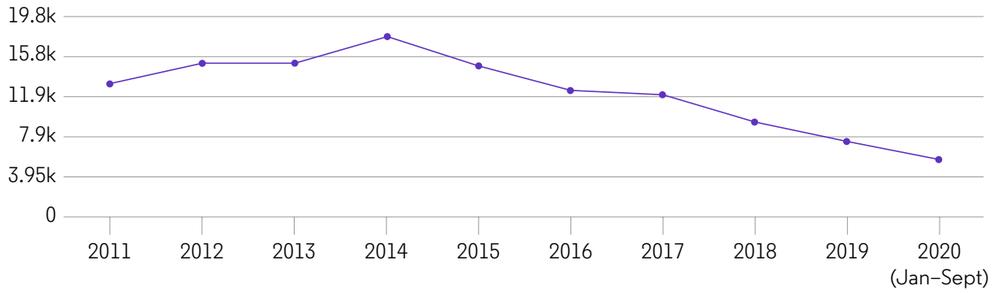
## About BROVANA® in the market

- Four tentative ANDA filings in the United States: Axar Pharmaceuticals Inc, Lupin Limited, Cipla Limited, Teva Pharmaceutical Industries Ltd
- According to the U.S. FDA, eligibility extinguished for the 180-day generic drug exclusivity for a generic version of BROVANA®
- Despite the generic interest, declining U.S. market share (2017–2019):
  - -37% prescription count
  - -50% dose units count
  - Similar trend observed for other products in this therapeutic class since 2017

## About Sunovion Pharmaceuticals Inc.

- Holder of 11 U.S. FDA NDA filings between 2000 and 2020
- Marketer of nine products in the United States: two under litigation (eslicarbazepine acetate and levalbuterol tartrate) and one to lose exclusivity on Dec 16, 2031 (apomorphine hydrochloride)
- December 2016: agreement to commercialize Novartis' three COPD products, UTIBRON NEOHALER® (glycopyrronium; indacaterol maleate), SEEBRI NEOHALER® (glycopyrronium) and ARCAPTA NEOHALER® (indacaterol maleate), in the United States
- July 2017: divested U.S. marketing rights of ALVESCO®, OMNARIS® and ZETONNA® against asthma and allergic rhinitis to Covis Pharma

**Market share history**
**Prescriptions**




**BROVANA®**
**(arformoterol tartrate)**
Respiratory – chronic obstructive pulmonary disease

**~59m**

people have COPD in the key markets (United States, France, United Kingdom, Germany, Spain, Italy, Japan)

## Patient impact

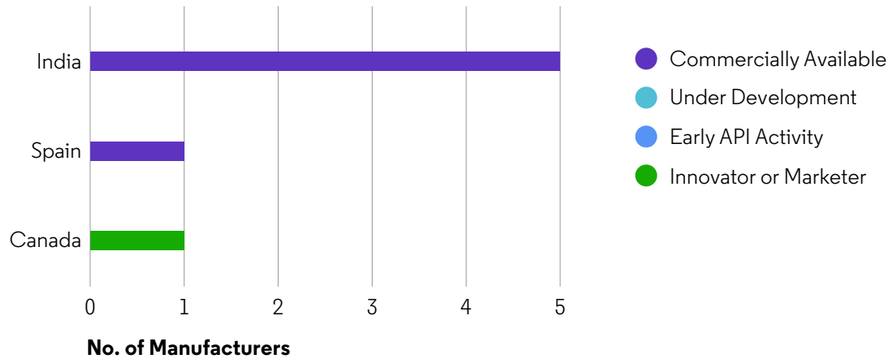
COPD is a chronic disease requiring lifelong treatment; as such, it is associated with high economic and patient burden due to lost productivity, healthcare expenditure and reduced quality of life. Treatment with either a LABA or a long-acting muscarinic antagonist (LAMA) is the preferred first-line therapy. With worsening symptoms, polypharmacy, potentially requiring a multi-inhaler regimen, is common and can be expensive and difficult for patients to manage.

**U.S. generics forecast**


**API availability**


**API manufacturers**

**Manufacturers by top countries**




Based on Cortellis data, active pharmaceutical ingredients (API) are available for regulated markets from multiple manufacturers.

**Source:** Cortellis Generics Intelligence. Data current as of April 21, 2021

# Januvia

**What to watch: Will Merck settle with more generic filers? How many generic entrants will we see, and how quickly will prices erode for this top-selling drug?**

**About JANUVIA®**

- Marketed by Merck & Co
- Dipeptidyl peptidase-4 (DPP-IV) inhibitor to treat type 2 diabetes

**JANUVIA®**
**(sitagliptin phosphate)**
Endocrine – type 2 diabetes

**2006**

First U.S. approval date:
October 16, 2006

**2007**

First E.U. approval date:
March 21, 2007

**2022**

U.S. 30-month stay expiries:
2022–2023

**2022**

E.U. Supplementary protection certificate (SPC) expiries: 2022

**2026**

Japan patent expiries: 2026

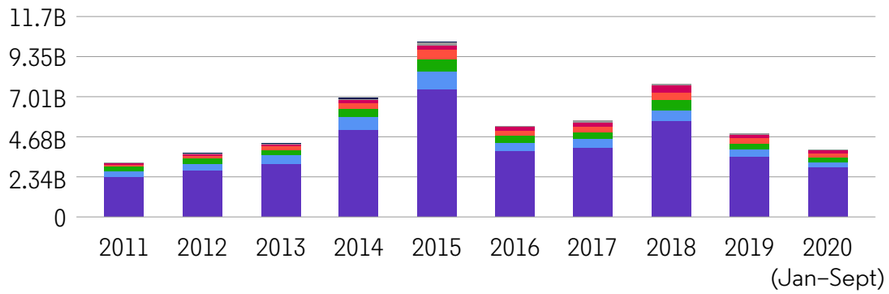
## About JANUVIA® in the market

- In litigation in the United States, as of 2021
- Blockbuster status due to its weight-neutral mechanism of action (MOA) and excellent safety and tolerability
- According to the FDA, six ANDAs for generic versions of JANUVIA® filed on the first day possible and eligibility for the 180-day generic drug exclusivity potentially shared by multiple companies
- Eight tentative ANDA approvals and eight additional ANDA filings
- According to Merck, with its sitagliptin patent settlement agreements, companies potentially able to bring their products to market in November 2026 or earlier under certain circumstances

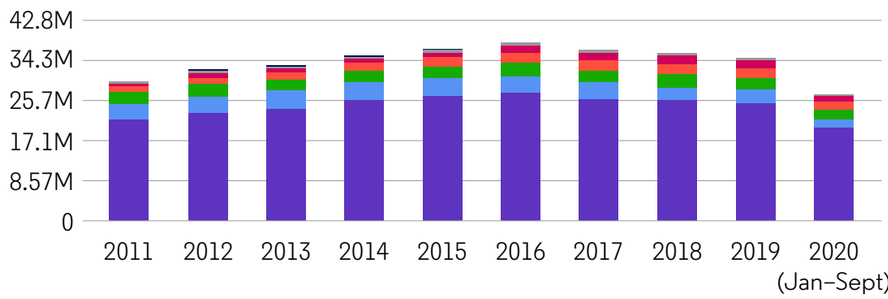
## About Merck & Co (United States and Canada; MSD elsewhere)

- Main markets: oncology, vaccines, infectious diseases and cardiometabolic disorders
- Additional products in their type 2 diabetes type II portfolio: STEGLUJAN® (ertugliflozin, sitagliptin phosphate), STEGLATRO® (ertugliflozin), SEGLUROMET® (ertugliflozin, metformin) and JANUMET® (sitagliptin, metformin) and its long- release version.
- In April 2013, Merck & Co agreement to develop and commercialize Pfizer's ertugliflozin, as well as ertugliflozin/metformin and ertugliflozin/sitagliptin combinations for type 2 diabetes worldwide, excluding Japan

**Top competitors**
**Dose units**




**Top competitors**
**Prescriptions**




**Active Ingredient**

- metformin hydrochloride
- glimepiride
- sitagliptin phosphate
- liraglutide
- saxagliptin hyrochloride
- linagliptin
- nateglinide
- pramlintide acetate
- dapagliflozin propanediol
- Other

**JANUVIA®**
**(sitagliptin phosphate)**
Endocrine – type 2 diabetes

**~78m**

adults have type 2 diabetes in the key markets

## Patient impact

Because DPP-IV inhibitors have excellent safety and tolerability profiles, physicians are willing to prescribe them as adjunctive therapy for a wide range of patients, including those with early-stage disease and elderly patients at risk of hypoglycemia.

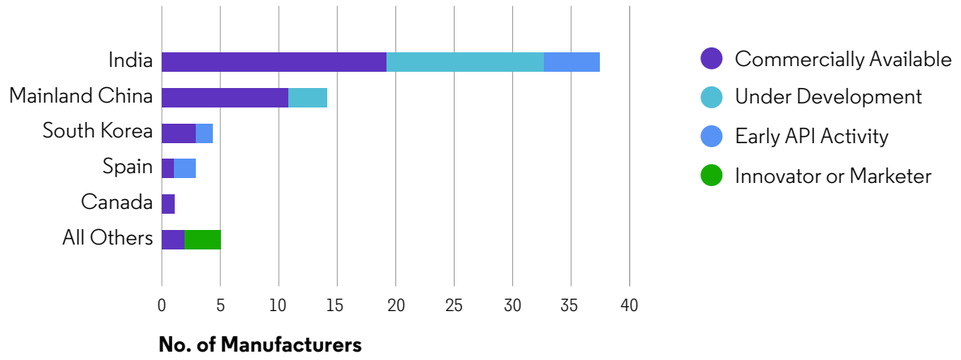
They are also being increasingly used as a first-line option in patients who cannot tolerate metformin. However, cost is currently an issue, so physicians are frequently restricted to prescribing this drug class to patients who have already failed less-costly therapies such as metformin and the sulfonylureas.

**U.S. generics forecast**


**API availability**


**API manufacturers**

**Manufacturers by top countries**




Based on Cortellis data, API is excessively available, primarily from manufacturers in India and Mainland China.

**Source:** Cortellis Generics Intelligence. Data current as of April 21, 2021

# Humira

**What to watch: Will the U.S. market share for HUMIRA® trend as it has in the European Union,or will we see significant price erosion with the introduction of numerous biosimilars?**

**About HUMIRA®**

- Patented by AbbVie Inc.
- TNF-inhibitor to treat many autoimmune conditions with inflammation as a central mechanism, including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, plaque psoriasis, juvenile idiopathic arthritis, ulcerative colitis, moderate to severe hidradenitis suppurativa and more

**HUMIRA® (adalimumab)**
Excessive immune response/
autoimmunity

**2002**

First U.S. approval date:
December 31, 2002

**2003**

First E.U. approval date:
April 16, 2003

**2023**

U.S. settlement agreements for biosimilar entry: September 30, 2023 – December 15, 2023

## About HUMIRA® in the market

- Experienced an increase in global sales by 10.5%, from year ending 2019 to year ending 2020
- Several aBLA filings in the United States: Alvotech, Amgen Inc, Boehringer Ingelheim, Coherus BioSciences, Mylan NV, Pfizer Inc, Samsung Bioepis Co Ltd and Sandoz
- Settlement agreements between AbbVie and several companies regarding adalimumab biosimilar products
- In the European Union, there are numerous biosimilar products available in the market, although the market share for HUMIRA still dominant

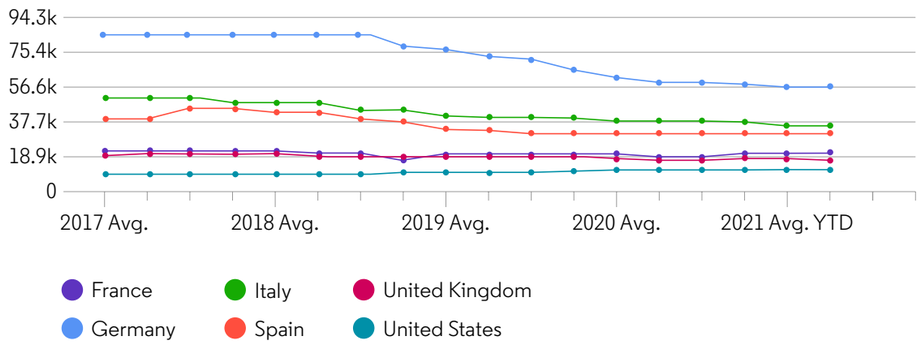
Pricing trends in the United States and European Union, for wholesale price based on the average price of all available pack sizes within the selected country

## About AbbVie Inc.

- Portfolio focused on immunology, oncology, neuroscience, virology, eye care and aesthetics
- Immunology portfolio: HUMIRA® (adalimumab), RINVOQ® (upadacitinib) and SKYRIZI® (risankizumab-rzaa)
- Upadacitinib ($629.1 million worldwide in 2020) losing exclusivity in 2029 for major European markets and Japan and in 2031 for the United States
- Risankizumab-rzaa ($1,625 million worldwide in 2020) losing exclusivity beyond 2030 in all main regulated markets

### Country comparison

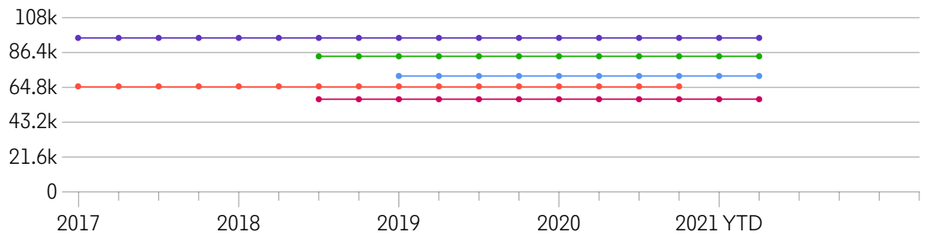
**USD**




Pricing trends in the United States and European Union, for wholesale price based on the average price of all available pack sizes within the selected country

### Historical prices

**USD**




**Trade Name and Pack Size**

- Abbvie Humira (Injection 40 MG 0.8 ML 6 Prefilled Pen)
- Abbvie – Humira (Injection 40 MG 0.8 ML 6 Prefilled Syringe)
- Amgen – Amgevita (Injection 40 MG 0.8 ML 6 Prefilled Pen)
- Amgen – Amgevita (Injection 40 MG 0.8 ML 6 Prefilled Syringe)
- Sandoz – Hyrimoz (Injection 40 MG 0.8 ML 6 Prefilled Pen)
- Sandoz – Hyrimoz (Injection 40 MG 0.8 ML 6 Prefilled Syringe)
- Amgen – Amgevita (Injection 40 MG 0.8 ML 4 Prefilled Pen)
- Abbvie – Humira (Injection 40 MG 0.8 ML 4 Prefilled Syringe)
- Amgen – Amgevita (Injection 40 MG 0.8 ML 4 Prefilled Pen)
- Amgen – Amgevita (Injection 40 MG 0.8 ML 4 Prefilled Syringe)

Ex-manufacturer price in Italy based on launched packs

**HUMIRA® (adalimumab)**
Excessive immune response/
autoimmunity

**15–30m**

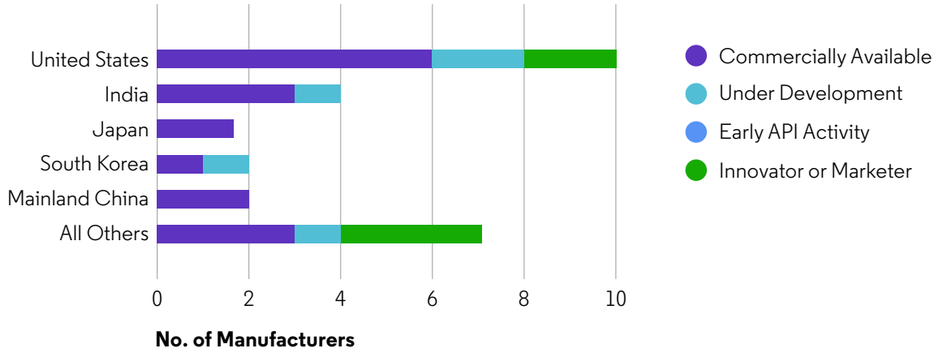
people in the United States
have an autoimmune disease

## Patient impact

A generic option could provide a more cost-effective treatment option for the many patients across rheumatology, dermatology and gastroenterology, particularly given the high cost of HUMIRA.

### API manufacturers

**Manufacturers by top countries**




Based on Cortellis data, API is available for regulated markets from manufacturers in the United States and Asia.

### API availability


**Source:** Cortellis Generics Intelligence. Data current as of April 21, 2021

# Vemlidy

**What to watch: Will licensing agreements impact the timing of generic entrants? Will the generic availability of VIREAD® impact market performance and interest?**

**About VEMLIDY®**

- Patented by Gilead Sciences Inc.
- Anti-HBV reverse transcriptase inhibitor to treat chronic hepatitis B viral (HBV) infection

**VEMLIDY®**
**(tenofovir alafenamide)**
Infectious diseases –
HIV, hepatitis B

**2015**

First E.U. approval date:
November 19, 2015

**2016**

First U.S. approval date:
November 10, 2016

**2021**

Japan re-examination period
expiry: December 19, 2021

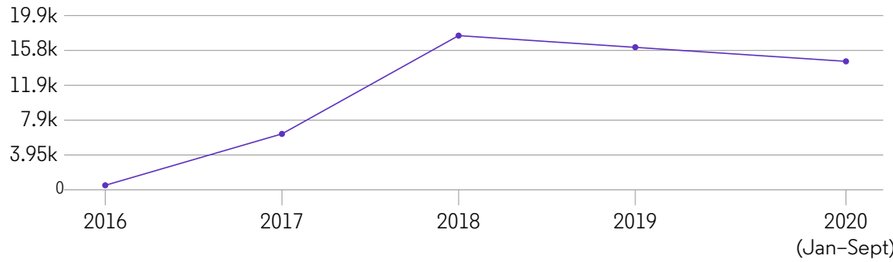
## About VEMLIDY® in the market

- Under litigation in the United States, with six ANDA filings: Apotex Inc, HEC Pharm Group, Hetero Drugs Limited, Laurus Labs, Lupin Limited and Shilpa Medicare Ltd
- In May 2023, expiry of the stay of FDA approval concerning the ANDAs in the United States
- Experienced an increase in global sales by 28.5%, from year ending 2019 to year ending 2020

## About Gilead Sciences Inc.

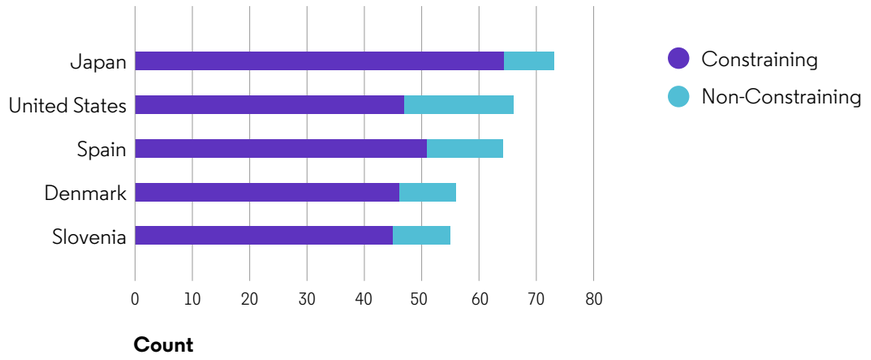
- Gilead commercializes prescription products for several therapeutic areas including HIV/AIDS, liver diseases, serious respiratory and cardiovascular conditions, cancer and inflammation.
- Marketed products for liver diseases: EPCLUSA® (sofosbuvir, velpatasvir), HARVONI® (ledipasvir, sofosbuvir), HEPSERA® (adefovir dipivoxil), SOVALDI® (sofosbuvir), VIREAD® (tenofovir disproxil fumarate), VOSEVI® (sofosbuvir, velpatasvir, voxilprevir) and VEMLIDY® (tenofovir alafenamide)
- In the main regulated markets, generic versions only for HEPSERA® and VIREAD®

**Market share history**
**Prescriptions**




## Japan has the highest number of constraining patents

**Unexpired patents**
**Top 5 patent territories**




**Source:** Cortellis Generics Intelligence

**VEMLIDY®**
**(tenofovir alafenamide)**
Infectious diseases –
HIV, hepatitis B

**~2.5m**

people in the United States and Europe have HBV infection

## Patient impact

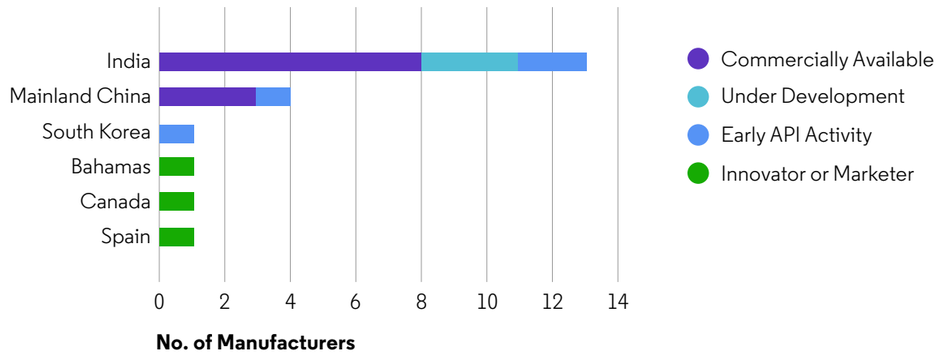
Patients with a chronic HBV infection experience slow disease progression, and initiation of therapy can be delayed based on patient characteristics and evidence of active viral replication. However, once on treatment, patients with HBV are often on lifelong daily therapy to maintain viral suppression and prevent the detrimental long-term effects of untreated infections like hepatitis flares and liver damage. When choosing an appropriate treatment, the cost of long-term therapy is an important consideration by physicians, in addition to safety and tolerability.

**U.S. generics forecast**


**API availability**


**API manufacturers**

**Manufacturers by top countries**




Based on Cortellis data, API is excessively available, primarily from manufacturers in India and Mainland China. Gilead granted non-exclusive rights for a number of companies to manufacture to ensure access to anti-viral medicines to address unmet medical needs.

**Source:** Cortellis Generics Intelligence.
Data current as of April 21, 2021

# Xarelto

**What to watch: How many generic entrants will we see? Will any litigation settlements be disclosed, and how quickly will prices erode for this top-selling drug?**

**About XARELTO®**

- Patented by Bayer Healthcare AG, marketed by Janssen in the United States
- Factor XA inhibitor used to treat and prevent blood clots, which may lower the risk of stroke, deep vein thrombosis (DVT), pulmonary embolism (PE) and similar conditions

# Market overview

**2008**

First E.U. approval date:
September 30, 2008

**2011**

First U.S. approval date:
July 1, 2011

**2023**

Constraint Date Forecast:
2023 (E.U. Top 5)
2024 (U.S., Japan)

**XARELTO®**
**(rivaroxaban)**
Cardiovascular – Stroke, deep vein thrombosis (DVT), pulmonary embolism (PE)

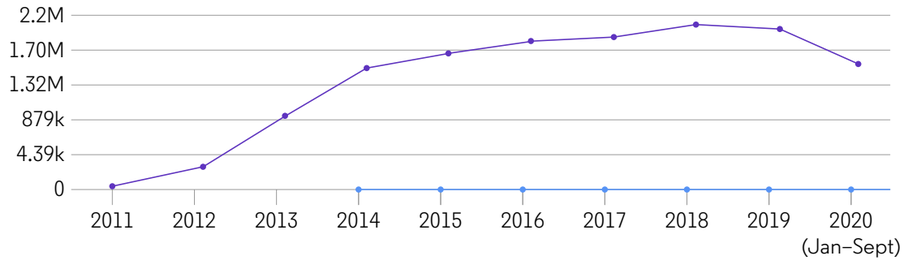
## About XARELTO® in the market

- Seventeen ANDA filings, with three tentative approvals
  - Eight ANDAs filed on the first day possible and may share eligibility for the 180-day generic drug exclusivity
  - Four ANDAs for the 2.5 mg tablet filed on the same day and may share eligibility for the 180-day generic drug exclusivity for that strength
- 2020 sales:
  - Global sales: $11.6 billion
  - Highest U.S. sales of all LOE products reviewed: $6.5 billion

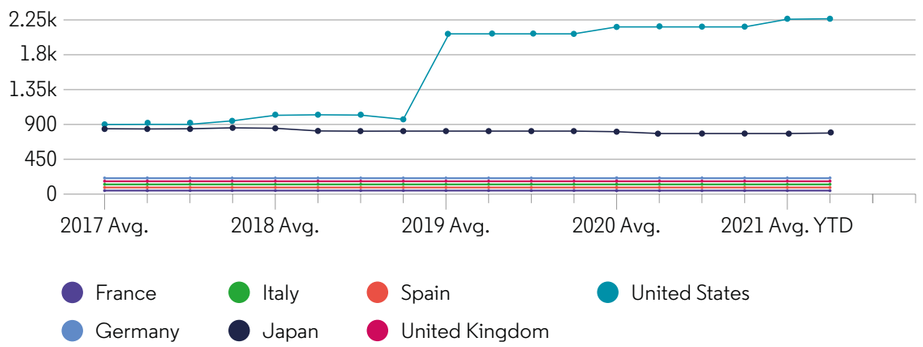
## About Bayer Healthcare AG

- Products for cardiology, oncology, ophthalmology, hematology, women's health and infectious diseases therapeutic areas
- Cardiology portfolio: XARELTO® (rivaroxaban), ADALAT® (nifedipine), ADEMPAS® (riociguat) and VERQUVO® (vericiguat)
- Riociguat ($303.5 million worldwide in 2020) currently in litigation in the United States and losing exclusivity in 2028 in the European Union top five and Japan
- Vericiguat under development with Merck & Co. and just approved in the United States in January 2021

**Market share history**
**Prescriptions**




**Current pricing trends across the United States, European Union top five and Japan (considers average pack size, ex manufacturer list price)**
**USD**




**Source:** Cortellis Generics Intelligence

**XARELTO®**
**(rivaroxaban)**
Cardiovascular – Stroke,
deep vein thrombosis (DVT),
pulmonary embolism (PE)

**~13m**

people have peripheral arterial disease in the key markets

## Patient impact

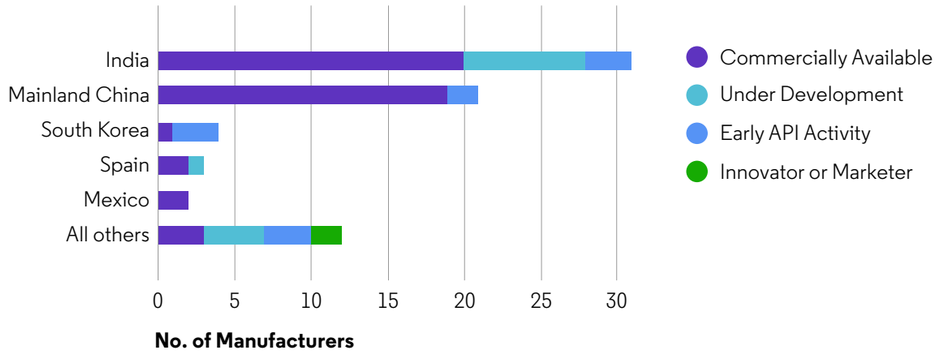
Given the many indications treated with Xarelto, the impact of generic options could be significant, providing access to this treatment for a larger proportion of patients. For peripheral artery disease, the launch of branded agents might encourage companies to adopt an aggressive approach to increasing awareness of the disease among patients and physicians, leading to earlier diagnosis and better outcomes.

**U.S. generics forecast**


**API availability**


**API manufacturers**

**Manufacturers by top countries**




**Source:** Cortellis Generics Intelligence.
Data current as of April 21, 2021

# Calquence

**What to watch: How many ANDA filers with paragraph IV certification will file later this year?**

**About CALQUENCE®**

- Patented by AstraZeneca
- Inhibitor of Bruton's tyrosine kinase (BTK) with potential antineoplastic activity to treat CLL, SLL and previously treated MCL

# Market overview

**CALQUENCE® (acalabrutinib)**
Oncology – mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), small lymphocytic leukemia (SLL)

## 2017

First U.S. approval date:
October 31, 2017

## 2020

First E.U. approval date:
November 5, 2020

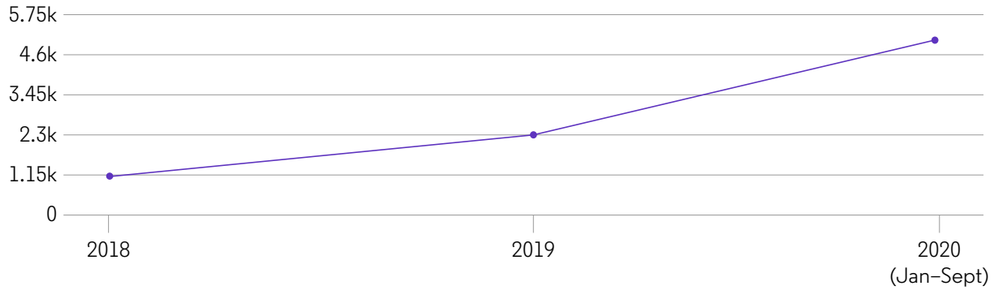
## About CALQUENCE® in the market

- Global 2020 sales: More than $500 million, up from $164 million in 2019
- In the United States, increase in market share by 115% from 2018 to 2019

## About AstraZeneca

- Main focus: oncology, cardiovascular, renal and metabolism, and respiratory and immunology
- Except for a bevacizumab biosimilar and legacy products such as ZOLADEX® (goserelin acetate), almost all their oncology portfolio (accounting for 42% of their revenue) are recently approved drugs that will lose exclusivity within the next 15 years

**Market share history**
**Prescriptions**




**CALQUENCE® (acalabrutinib)**
Oncology – mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), small lymphocytic leukemia (SLL)

**~50,000**

people have MCL, CLL or SLL in the key markets

## Patient impact

Approximately 70% of MCL cases are diagnosed with advanced disease, and most patients receive treatment regardless of disease stage. Because of the aggressive nature of MCL, few patients experience an extremely durable remission, while most patients will require second or third-line treatment. Although patients with CLL or SLL do not necessarily receive pharmacologic treatment initially, 75% of patients eventually require drug treatment.

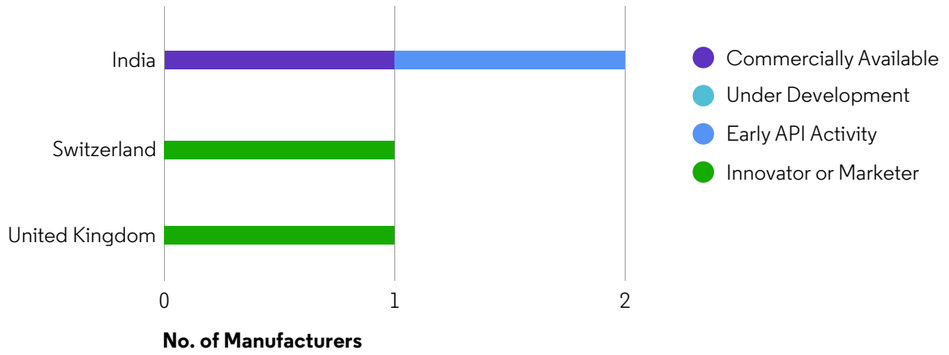
Based on Cortellis data, there are few confirmed sources of API, although there are companies in India (all with an "Established" Corporate API Rating*) developing on the API: MSN Laboratories Private Limited, NATCO Pharma Limited, Sun Pharmaceutical Industries Ltd. and Sionc Pharmaceuticals Pvt. Ltd. Although there is minimal API manufacturing, Cortellis Generics Intelligence data show a variety of patents on manufacturing process, intermediates and product derivatives from the following companies indicating numerous generic companies evaluating the product:

- **Apotex Inc.**
- **Alembic Pharmaceuticals Limited Cipla Limited**
- **Dr. Reddy's Laboratories**
- **Fresenius SE & Co. KGaA**
- **Teva Pharmaceutical Industries Ltd.**
- **Zentiva Group, a.s.**

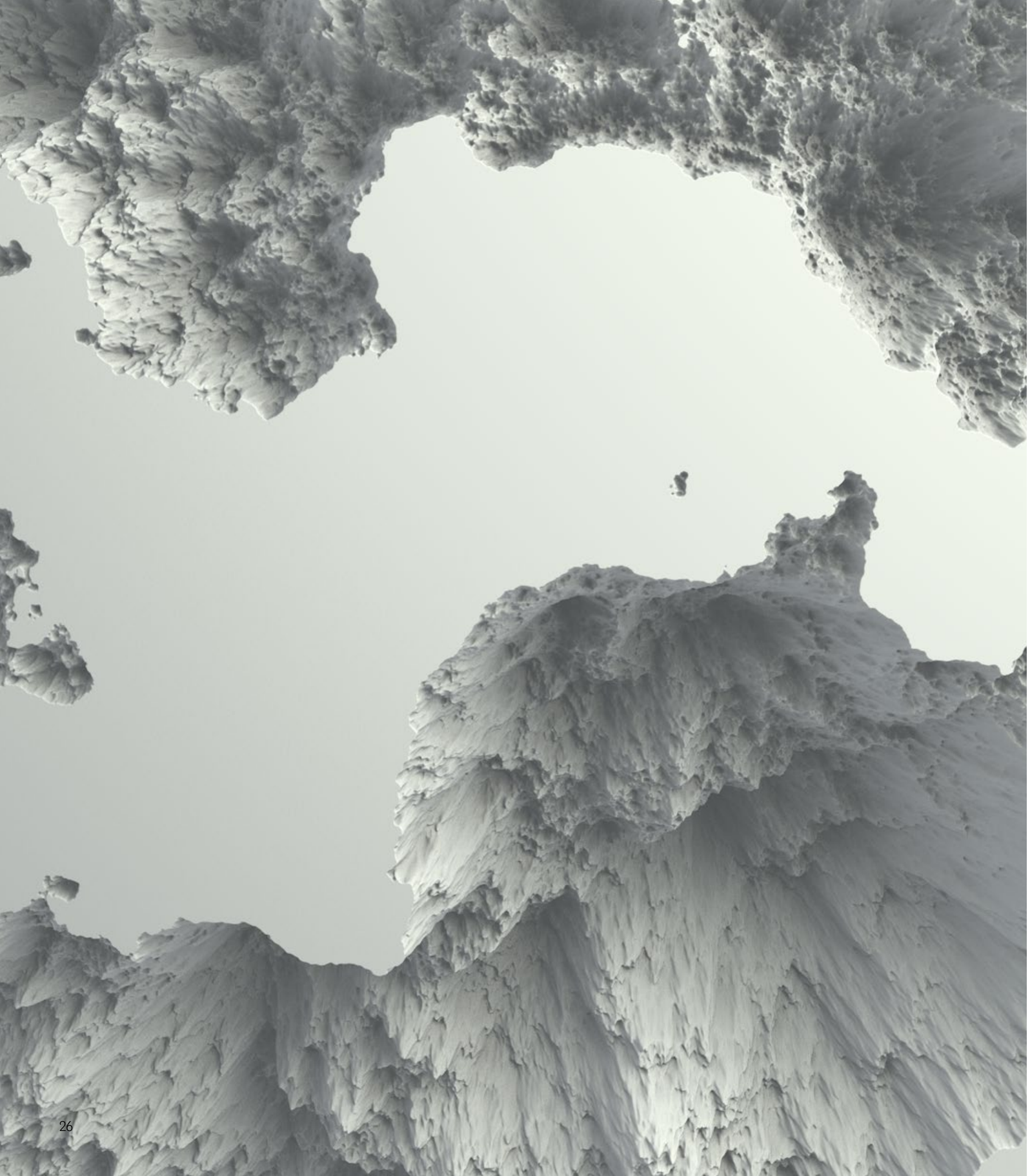
**U.S. generics forecast**


**API availability**


**API manufacturers**
**Manufacturers by top countries**




**Source:** Cortellis Generics Intelligence. Data current as of April 21, 2021



# Antineoplastic landscape

Oral or intravenous administration of antineoplastic drugs in cancer management aims to prevent or cure cancer, prevent or slow the growth of a tumor or manage symptoms (palliation).

Growth in the antineoplastic market is driven by the demand for effective medications to treat the increasing global incidence of cancer, while the growth of the generic antineoplastic market is driven by the demand for cost-effective treatments. Although a shift toward personalized medicine in oncology presents opportunities for manufacturers, the high cost and heterogenous nature of cancer are limiting factors.

Of the more than 100 molecules with LOE in the antineoplastic therapy area in the United States, European Union top five or Japan between 2021 and 2027, nine molecules are experiencing loss of exclusivity across all three markets during that time frame.

## 2020 global sales per molecule:

- Olaparib – $1.6 billion
- Nilotinib hydrochloride – $1.6 billion
- Pazopanib – $570 million
- Ponatinib hydrochloride – $350 million
- Eribulin – $360 million
- Afatinib dimaleate – $370 million
- Ceritinib – $61 million
- Vorinostat – $14 million
- Vandetanib – $33.3 million

On the following pages, we detail the six antineoplastics with the highest global sales in 2020.

# LYNPARZA®
## Olaparib

### Poly ADP ribose polymerase (PARP) inhibitor

Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, metastatic breast, metastatic pancreatic or primary peritoneal cancer who have had complete or partial response to platinum-based chemotherapy

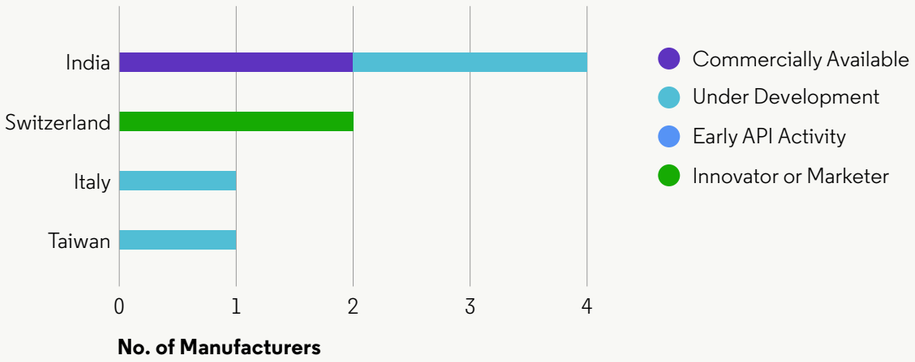
**Approvals and patent:**
- First E.U. approval: December 16, 2014
- First U.S. approval: December 19, 2014
Marketed by AstraZeneca

**Constraint date forecast:**
- Orphan Drug Exclusivity expiry: 2024 (United States)
- SPC expiries: 2029 (European Union)
- Patent expiries: 2024 (Japan)

### API availability


### API manufacturers

**Manufacturers by top countries**




# TASIGNA®
## Nilotinib hydrochloride

### Orally bioavailable aminopyrimidine-derivative Bcr-Abl tyrosine kinase inhibitor

Treatment of adult and pediatric patients with newly diagnosed or treatment-resistant Philadelphia chromosome–positive chronic myeloid leukemia (Ph+ CML)

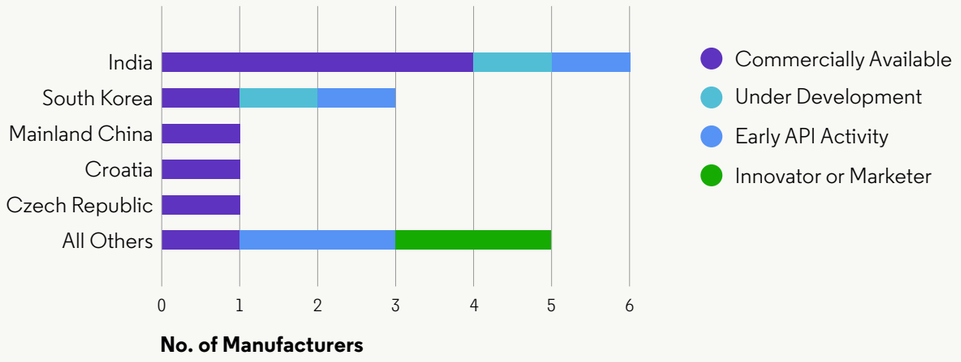
**Approvals and patent:**
- First E.U. approval: November 19, 2007
- First U.S. approval: October 29, 2007
- Marketed by Novartis Pharmaceuticals Corporation

**Constraint date forecast:**
- Patent expiry: 2023 (United States)
- Patent expiry: 2023 (European Union)
- Patent expiry: 2028 (Japan)

### API availability


### API manufacturers

**Manufacturers by top countries**



# VOTRIENT®
## Pazopanib

### Selective multi-targeted receptor tyrosine kinase inhibitor

Treatment of advanced renal cell carcinoma (RCC) and advanced soft tissue sarcoma

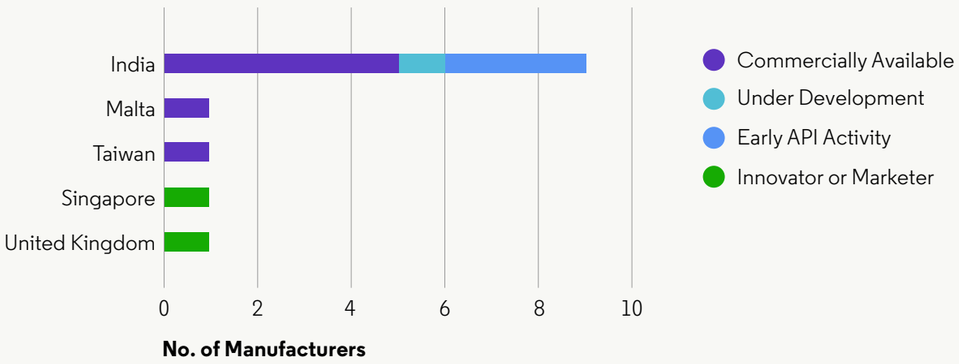
**Approvals and patent:**
- First E.U. approval: June 14, 2010
- First U.S. approval: October 19, 2009
- Marketed by Novartis Pharmaceuticals Corporation (United States and European Union) and GlaxoSmithKline plc (Japan)

**Constraint date forecast:**
- Patent expiry: 2023 (United States)
- SPC expiries: 2025 (European Union)
- Patent expiry: 2027 (Japan)

### API availability


### API manufacturers

**Manufacturers by top countries**




# ICLUSIG®
## Ponatinib hydrochloride

### Orally bioavailable Bcr-Abl tyrosine kinase inhibitor

Treatment of adult patients with treatment-resistant or intolerant chronic phase (CP) chronic myeloid leukemia (CML), accelerated phase (AP) or blast phase (BP) CML or Philadelphia chromosome–positive (Ph+) CML for which no other kinase inhibitors are indicated, and T315I-positive CML or T315I-positive Ph+ ALL

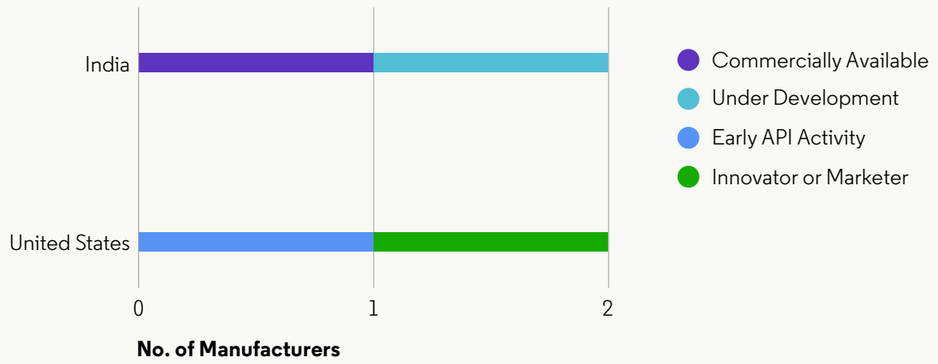
**Approvals and patent:**
- First U.S. approval: December 14, 2012
- First E.U. approval: July 1, 2013
- Marketed by Takeda Pharmaceutical Company Limited

**Constraint date forecast:**
- Patent expiry: 2026 (United States)
- Patent expiry: 2027 (Japan)
- SPC expiry: 2028 (European Union)

### API availability


### API manufacturers

**Manufacturers by top countries**



# HALAVEN®
## Eribulin

### Microtubule dynamics inhibitor

Treatment of refractory, metastatic breast cancer and liposarcoma

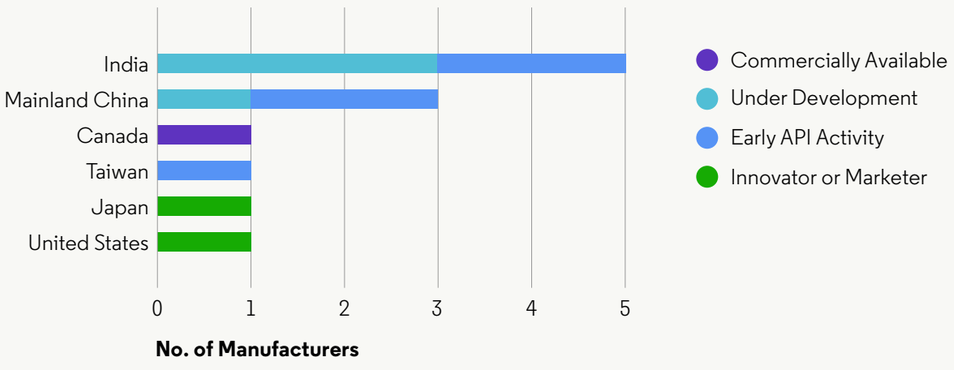
**Approvals and patent:**
- First U.S. approval: November 15, 2010
- First E.U. approval: March 17, 2011
- Marketed by Eisai Inc.

**Constraint date forecast:**
- Patent expiry: 2023 (United States)
- SPC expiry: 2024 (European Union)
- Patent expiry: 2024 (Japan)

### API availability


### API manufacturers

**Manufacturers by top countries**




# GILOTRIF®
## Afatinib dimaleate

### Orally bioavailable anilino-quinazoline derivative and inhibitor of the receptor tyrosine kinase (RTK) epidermal growth factor receptor (ErbB; EGFR) family

First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations

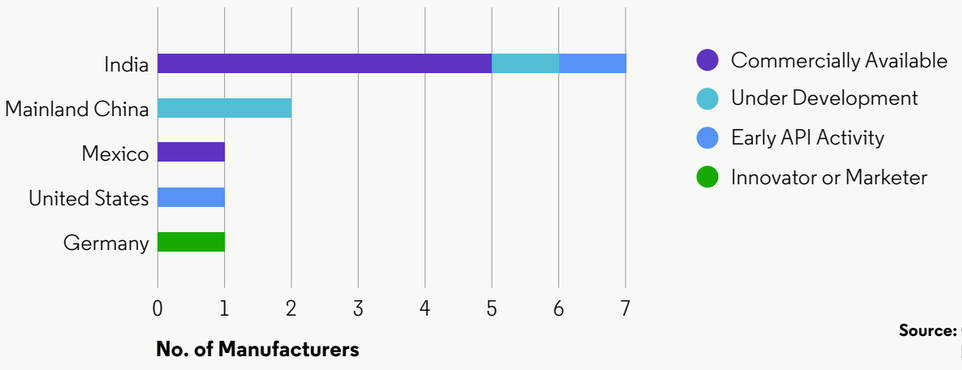
**Approvals and patent:**
- First U.S. approval: July 12, 2013
- First E.U. approval: September 25, 2013
- Marketed by Boehringer Ingelheim Pharmaceuticals, Inc

**Constraint date forecast:**
- Patent expiry: 2026 (United States)
- SPC expiry: 2026 (European Union)
- Patent expiry: 2026 (Japan)

### API availability


### API manufacturers

**Manufacturers by top countries**




**Source:** Cortellis Generics Intelligence.
Data current as of April 21, 2021

# Looking ahead

## A post-pandemic world needs more affordable alternatives and stronger supply chains

Generics and biosimilars are poised to play a key role in meeting patient needs as the world's economies and health systems recover.

The generics and biosimilars ecosystem is expected to grow larger and more diverse over the next few years,shaped by financial pressures on payers and manufacturers alike.

- **Still greater demand for cheaper treatments:** As the world emerges from the worst of the COVID-19 pandemic, with economies frayed and financial reserves and supply lines strained, demand for generic drugs and biosimilars is likely to grow.[17] Governments and commercial payers will be hard-pressed to trim spending on prescription drugs, even as a wave of revolutionary (and accordingly expensive) cancer treatments comes online and aging populations increase need in major markets.[18]

- **Shoring up generic supply chains:** Severe drug shortages in the early months of the pandemic exposed significant vulnerabilities in the global supply chain, particularly for generic drugs,[19] with manufacturing of APIs concentrated in Mainland China and India and supply lines breaking down as countries across the world went into lockdowns. Companies may need to validate alternative sources of these components to safeguard against future, global disruptions.

- **Continuing expansion of the biosimilars marketplace:** Biopharma giants like Pfizer and Amgen are joining smaller upstarts in the hunt to provide alternatives to expensive branded biologics.[20,21] We expect legacy biologics companies to use their scale, expertise and manufacturing capabilities to take on more nimble competitors and offset losses of their own off-patent biologics.[22] Looming patent expirations in key categories like anti-TNFs could create opportunities for small and large players alike.

- **Potential for patients to benefit:** Patients will likely have increased access to specialty treatments that were, prior to generic or biosimilar competition, prohibitively expensive for most patients in many markets.

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## About Clarivate

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