ULCERATIVE COLITIS - GLOBAL DRUG FORECAST AND MARKET ANALYSIS TO 2022 - EVENT-DRIVEN UPDATE
Executive Summary

The table below presents the key metrics for ulcerative colitis (UC) in the 10 major pharmaceutical markets analyzed in this report during the forecast period from 2012–2022: the US, France, Germany, Italy, Spain, the UK, Japan, Canada, China, and India.

### Ulcerative Colitis: Key Metrics in the 10 Major Pharmaceutical Markets, 2012–2022

#### 2012 Epidemiology
- Prevalent Population in the 7MM, Canada, China, and India: 1,861 million
- Treated Population in the 7MM, Canada, China, and India: 1,544 million

#### 2012 Market Sales
- US: $2,246m
- 5EU: $1,407m
- Japan: $64m
- Canada: $241m
- China and India: $225m
- Total Global: $4,182m

#### Pipeline Assessment
- Number of drugs in Phase I–II: 46
- Number of first-in-class drugs: 2

#### Most Promising Pipeline Drugs
- Entyvio [vedolizumab (Takeda)]: $1,423m
- Xeljanz [tofacitinib (Pfizer)]: $101m
- Kappaproct [DIMS 0150 (InDeX Pharmaceuticals)]: $25m

#### Key Events (2012–2022)
- Approval of first infliximab biosimilar in September 2013: ↓
- Simponi (golimumab) entering the US market in 2013: ↑↑
- Entyvio entering the US and EU in 2014: ↑↑↑
- Remicade (infliximab) losing patent 2018 (US), 2015 (EU): ↓↓↓
- Humira (adalimumab) losing patent in 2016 (US), 2018 (EU): ↓↓

### 2022 Market Sales
- US: $3,489m
- 5EU: $2,068m
- Japan: $169m
- Canada: $395m
- China and India: $618m
- Total Global: $6,740m

Source: GlobalData

Global = US, France, Germany, Italy, Spain, UK, Japan, Canada, China, and India; 5EU = France, Germany, Italy, Spain, and UK; 7MM = US, 5EU, Japan

Sales for UC by Region, 2012–2022

During the forecast period from 2012–2022, the growth of the UC market will be driven largely by the entry of Simponi and Entyvio, which will favor the increased uptake of biologics in the US, 5EU, Japan, and Canada. Although the number of UC prevalent cases is plateauing in the West, globally, the number of cases is rising, a phenomenon that will contribute to market growth over the next decade. Another event affecting the market is the launch of biosimilars, given the patent expiry of the UC blockbusters, Remicade and Humira, in the US in 2018 and 2016, respectively. However, the lack of an established regulatory path for biosimilars in the US presages the slow uptake of these products in this market, which could limit their availability, and consequently, inhibit the growth of the UC market.
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Major growth drivers in the UC market over the forecast period include:

- Entry of Entyvio and Simponi into the market
- Increased overall number of patients being treated with biological therapies
- UC prevalence is plateauing in the West, but is on the rise in the East
- UC pipeline will be increasingly composed of gut-specific therapies
- A phenomenal amelioration in the educational level of gastroenterologists and patients regarding UC

Conversely, major barriers to the growth of the UC market include:

- Remicade and Humira losing patent protection in the mid-forecast
- The 5-aminosalicylate (5-ASA) segment of the UC market being dominated by generics
- Austerity measures favoring generic prescribing
- Biosimilars are predicted to face low uptake due to the lack of regulatory guidelines in some markets, such as the US
- Parallel trade in select UC markets

In 2012, GlobalData estimated that the global UC market reached $4.18 billion across the 10 healthcare markets covered in our forecast: the US, France, Germany, Italy, Spain, the UK, Japan, Canada, China, and India. By the end of the forecast period, in 2022, sales across these markets will grow steadily to reach $6.78 billion, representing a Compound Annual Growth Rate (CAGR) of 4.9% over the 10-year timeframe, which includes four new market entrants and the launch of biosimilars.

Figure below illustrates the global UC sales by region during the 10-year forecast period.
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Research and Development and Corporate Strategies

The UC market consists of a plethora of small-molecule drugs and tumor necrosis factor (TNF)-inhibiting biologics that offer relatively good safety and efficacy. The current research and development (R&D) efforts will result in the emergence of newer pharmaceuticals touting oral administration, more convenient dosing frequencies, novel mechanisms of action (MOAs), and improved safety profiles. Additionally, biosimilars for many of the current market leaders will be launched in all the major markets during the forecast period. As a result, it will be increasingly difficult for any one product to increase its market share in such a competitive space.

Johnson & Johnson (J&J) has been a dominant player in the UC market since 2006, due to the success of Remicade, an intravenous (IV) tumor necrosis factor-alpha (TNF-α) inhibitor. However, with Remicade’s patent expiry looming in 2015 (EU), 2016 (rest of the world [RoW]), and 2018 (US), J&J’s sales will slip by the end of the forecast period, from approximately $2.8 billion in 2012 to $2.0 billion in 2022. Therefore, J&J developed Simponi, a subcutaneous (SC) TNF-α inhibitor, which was launched in 2013 in the US and 5EU. This brand, which has better efficacy in UC than Abbvie’s Humira, will allow J&J to retain its positive standing in the UC market for a longer period of time.

AbbVie has also been a key player in the UC market. Humira, its TNF-α inhibitor, was approved for UC in 2012 in the US and 5EU, but was completely used off label in this indication beforehand. Like Remicade, Humira’s patent expiry is imminent: in 2016 (US), 2017 (Japan and Canada), and 2018 (5EU). As such, AbbVie’s sales will slip by the end of the forecast period, from $1.4 billion to $563m in 2022. The lack of UC products in its pipeline suggests that the company’s strong presence in the UC market will begin to fade.

Pfizer is currently developing three different drugs for the treatment of UC and is striving to re-enter the UC market. Xeljanz, a janus kinase (JAK) inhibitor, is its most advanced late-phase pipeline product, but got off to a bumpy start with two rejections by the European Medicines Agency (EMA) for the treatment of rheumatoid arthritis (RA) in July 2013. Nevertheless, it is still under development for UC and has shown with promising results. Pfizer is also conducting safety trials to prove that when Xeljanz is co-administered with the company’s cholesterol-lowering medication, Lipitor (atorvastatin), the main safety concern regarding high cholesterol levels with Xeljanz is diminished.

Takeda’s Entyvio, is forecast to have a slow start, but will gradually increase its market share. The drug has a remarkably safe profile for a biologic, and it has experienced moderate uptake since its launch in Q2 2014.
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Roche’s etrolizumab is a “me-too” drug to Entyvio, which is forecast to encroach on the SC therapies that are already used for UC, such as Humira and Simponi. Roche is promoting the drug as a better treatment for TNF-blocker-naïve patients.

Figure below provides an analysis of the company portfolio gap in UC during the forecast period, split by disease severity (mild to moderate and moderate to severe).

Unmet Needs in the UC Market

Most of the unmet needs in the treatment of UC lay within the clinical aspects of its management, rather than with environmental factors, as both physician and patient awareness of the disease are rising with the help of social media and relevant organizations, such as Crohn’s and Colitis UK, and the Crohn’s & Colitis Foundation of America (CCFA).

The clinical unmet needs in UC include the lack of a curative therapy, diagnostic markers for disease severity, biologic treatment personalization, and preventative medicine for lowering the associated colorectal cancer risk, as well as the need for steroid replacement and oral formulations, and for the management of infectious adverse events.

As noted by several key opinion leaders (KOLs) interviewed by GlobalData, the highest unmet need in the management of UC is that there is currently no available treatment on the market that is specifically targeted to severe UC patients. This leaves a high unmet need for a curative therapy for severe UC patients.

“[There is a] poor prognosis for severe people [UC patients,] who will need hospitalization. I include [patients treated with] TNF-blockers in this [group].”

[Outside US] key opinion leader, September 2013

This leads to the second highest unmet need in UC, which is the lack of disease severity prediction tools. Severity is a part of the UC spectrum that needs to be evaluated early in the course of the
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disease, following the first flare. Patients who are found to be positive for a severe disease prognosis can be monitored closely by means of endoscopy, frequent blood tests, food intolerance tests, and stress management.

Remaining Opportunity for New Market Entrants

As mentioned by several KOLs interviewed by GlobalData, there is currently no available treatment on the market that is specifically targeted to severe UC patients. All the drug treatments currently used have been clinically tested in UC based on immunosuppression, and for most, their first indication was RA or graft-versus-host disease (GVHD). Moreover, 10–20% of the total treated severe UC population will still undergo colectomy. This leaves a high unmet need for a curative therapy for severe UC patients.

Despite the increasing necessity of induction of disease remission being among the numerous unmet needs in UC, there are only a few drugs in the pipeline (pre-registration and Phase III) that directly address this problem. However, if these drugs are approved, the landscape of the UC market will be altered significantly, since Takeda’s Entyvio will challenge the established use of Remicade in UC, and InDex Pharmaceuticals’ Kappaproct is promising rapid induction of disease remission after only a single use. Both of these drugs are gut-specific and have remarkable safety profiles. Meanwhile, Pfizer’s Xeljanz might become a threat to the thiopurines, which are being used off label in UC, a practice that most gastroenterologists are wary about, since these drugs have an unpredictable adverse event profile. Therefore, having an immunosuppressive drug that has been specifically tested in UC and has a well-characterized safety profile will benefit severe UC patients.

Leading Pipeline Agents in the UC Treatment Paradigm and the Future Market Outlook

Following its anticipated approval and launch in early 2014, Entyvio is expected to reach blockbuster status and become a game-changer in UC, considering that it targets an integrin that is specific to the intestinal tissue. Kappaproct is currently in Phase III of development for the induction of remission in severe UC patients who are destined for colectomy.

Pfizer’s Xeljanz is anticipated to replace the thiopurines in UC; however, it is experiencing a bumpy start in its European regulatory process, since it was twice rejected by the EMA for its primary indication, RA, in April and July 2013. Regardless, if the Phase III trial results show that Xeljanz has a relatively manageable safety profile for the induction of remission in severe UC patients, it might become a threat to the thiopurines, since they show an unpredictable adverse event profile.

Focusing on the future outlook of the UC market following the entry of the aforementioned pipeline drugs, Entyvio is forecast to enter the US and EU
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markets in 2014. In the same year, Kappaproct is anticipated to enter the 5EU market. A few years later, in 2017, Xeljanz will be making its way to the US, 5EU, Canadian, and Japanese markets. As a result, the UC market will experience a surge of new therapies during the early forecast period. This will increase the number of therapy options that have the potential to modify the course of the disease, and, in turn, drive market growth. Specifically, Entyvio is expected to close the forecast period in 2022 with an estimated $1.3 billion, while Kappaproct will generate sales of $25m, and Xeljanz will reach a value of $99m. Figure below provides a competitive assessment of the late-stage pipeline agents in UC.

What Do Physicians Think?

Physicians interviewed by GlobalData expressed doubts about the use of Inflectra (an infliximab biosimilar) following its approval in Europe in September 2013.

“I do not comprehend what the EMA based the label extrapolation upon. I would like to see data from a clinical trial of Inflectra done on UC patients. I’m afraid, though, that we [physicians] might receive pressure to prescribe this biosimilar treatment because of the healthcare funding cuts”

[EU] key opinion leader, October, 2013

The physicians also underscored the need for a curative treatment for UC.

“Essentially, there is no adequate treatment for severe UC patients. AZA [azathioprine] has an unpredictable array of adverse effects and no guaranteed efficacy. The biologics only work in 40% of the severe UC patients, and in most cases, they are underdosed. We need a curative treatment.”

[EU] key opinion leader, October 2013

Some KOLs expressed the opinion that UC patients should be referred to a specialist before they develop bloody diarrhea, as well as the desire for companies to develop disease severity prediction tests, which could allow for the earlier detection of UC.
“Patients usually go to their primary care physicians and complain about chronic diarrhea, some sort of uveitis, poor quality of life, etcetera. If colonoscopy is considered necessary, and a heavy colonic inflammatory burden is observed, then the patient undergoes regular monitoring. This doesn’t happen with everyone, though, and in 90% of the cases, UC is diagnosed upon the presence of bloody diarrhea. But, I think we can catch it sooner. We need a [disease] severity prediction test.”

[US] key opinion leader, November, 2013

The physicians also commented on the clinical positioning that they would choose for Takeda’s pipeline therapy, Entyvio.

“[I think if vedolizumab is as good as it looks, it will be] a first- or second-line treatment in place of azathioprine. If you have a UC patient relapsing frequently, despite the use of mesalazine, vedolizumab will be an ideal candidate. I regard it as safer than azathioprine and more effective [for UC]. [However,] I would carry on using anti-TNFs for the treatment of CD.”

[EU] key opinion leader, September 2013

The physicians also shared their thoughts on the high risk of colorectal cancer in inflammatory bowel disease (IBD) sufferers, which includes those with UC.

“Colorectal cancer is a huge risk in UC patients....Pharmaceutical intervention is not designed to prevent this risk. The use of immunosuppressants does not help.”

[EU] key opinion leader, September 2013
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2 Introduction

2.1 Catalyst

The catalysts for this event-driven update report are to:

- Examine the impact that Entyvio’s (vedolizumab’s) May 2014 approval and launch in Q2 2014 (US and 5EU) will have on the future management of ulcerative colitis (UC) in these markets and the competitive landscape in terms of market value.

- On March 27, 2014, Roche registered a Phase III trial of etrolizumab to evaluate its efficacy and safety during induction and maintenance in patients with moderate to severe active UC who are refractory to or intolerant of tumor necrosis factor (TNF) inhibitors. In this report, GlobalData investigates the shift of the market to integrin inhibitors following the expected approval and launch of Roche’s “me-too” drug to Takeda’s Entyvio, etrolizumab.

- Assess the future of the currently marketed tumor necrosis factor (TNF)-blocking biologics, Remicade (infliximab) and Humira (adalimumab), following their loss of patent protection, the launch of new products, and the introduction of biosimilars into the market, with the first infliximab biosimilar, Celltrion’s Remsima being approved in the EU on September 16, 2013, and filed for approval with the FDA on August 12, 2014.

- Evaluate the significance of the late-stage pipeline products and how their launch will shape the future treatment landscape in UC.

- Identify the remaining unmet needs in UC and highlight untapped opportunities.

The launch of new biologic drugs will increase treatment options, improve disease management, and drive growth in the UC market. Although the need for safe and effective new treatments, let alone a curative drug, is paramount for patients with UC, the products that are currently in the pipeline are expected to face challenges in gaining patient share following their entry into the UC market. These new entrants will undergo pricing and reimbursement pressures and will also face fierce competition from infliximab and adalimumab biosimilars.

2.2 Related Reports

Introduction


2.3 Upcoming Related Reports

Appendix

11.8 About GlobalData

GlobalData is a leading global provider of business intelligence in the healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports, and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

GlobalData has offices in New York, San Francisco, Boston, London, India, Korea, Japan, Singapore, and Australia.

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