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GlobalData
PharmaPoint

CROHN'S DISEASE – GLOBAL DRUG FORECAST AND MARKET ANALYSIS TO 2022

Executive Summary

Crohn's Disease: Key Metrics in the Seven Major Pharmaceutical Markets	
2012 Epidemiology	
Diagnosed Prevalent Population – Global	1.3 million
Diagnosed Treated Population – Global	0.8 million
2012 Market Sales	
US	$2,126.1m
5EU	$396.9m
Japan	$227.8m
Total 7MM	**$2,750.8m**
Total Global	**$3,168.8m**
Pipeline Assessment	
Number of drugs in Phase III	4
Number of first-in-class drugs in the late-stage pipeline	3
Most Promising Pipeline Drugs	**Peak-Year Sales**
Entyvio (vedolizumab)	$659.2m
Stelara (ustekinumab)	$399.5m
Key Events (2012–2022)	**Level of Impact**
Entyvio launch in 2014 (US, EU)	↑↑↑
Remicade (infliximab) patent expiry in 2018 (US)	↓↓↓
Infliximab biosimilars launch in 2015 (EU)	↑↑
Stelara launch in 2015 (US, EU)	↑↑
Humira (adalimumab) patent expiry in 2016 (US)	↓↓↓
2022 Market Sales	
US	$2,871.3m
5EU	$457.5m
Japan	$288.2m
Total 7MM	**$3,617.0m**
Total Global	**$4,194.8m**

Source: GlobalData

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

Above mentioned table presents the key metrics for Crohn's disease (CD) in the seven major pharmaceutical markets analyzed in this report: the US, France, Germany, Italy, Spain, the UK, and Japan. Additional markets covered in this report include Canada, China, and India, for a total of 10 markets.

Launch of Non-Anti-TNF Drugs in the Near Term Will Fuel CD Market Growth to 2022

In 2012, GlobalData estimated that the global CD market was valued at $3.2 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 have grown steadily to reach $4.2 billion, representing a Compound Annual Growth Rate (CAGR) of 2.8% over the 10-year timeframe, which includes four new market entrants and the launch of biosimilars.

Major growth drivers in the CD market over the forecast period include:

- The anticipated launch of the first non-anti-tumor necrosis factor (TNF) biologics, such as Takeda's Entyvio and Johnson & Johnson's (J&J's) Stelara
- High unmet need within the anti-TNFrefractory patient group, which presents untapped market opportunities

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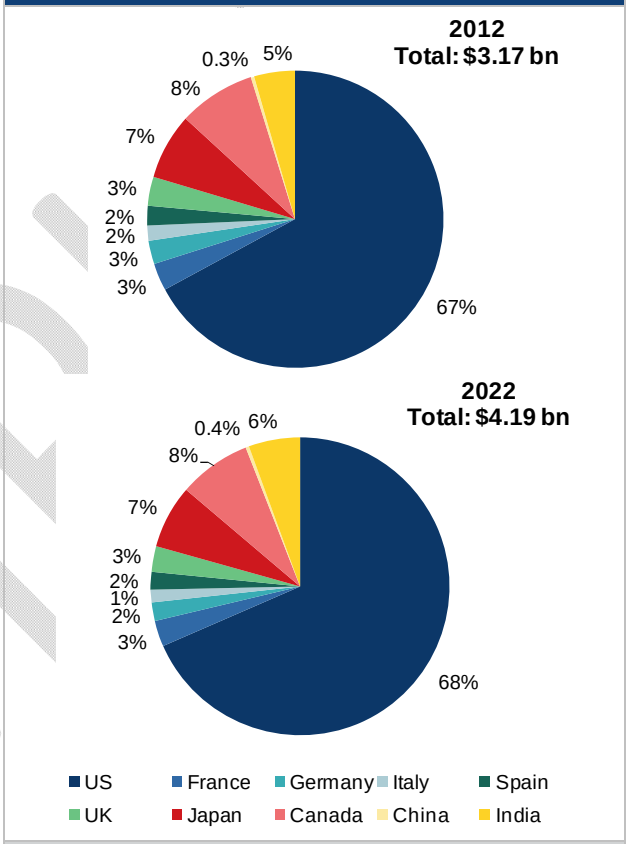
- The uptake of infliximab and adalimumab biosimilars to the detriment of their established branded biologics, Remicade and Humira, respectively
- Continued uptake of select biologic brands — namely, Remicade in the US, Japan, and Canada; and Humira in the US
- Increasing prevalent cases of CD
- Improved access to pharmacological therapies in China and India

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

- The fact that CD has an established biologics market, which creates a challenging environment for new market entrants
- Intensifying competition within the moderate-to-severe patient segment, as a number of new products are targeting this group
- Brand erosion following the patent expiry of the market-leading therapies, Remicade and Humira
- The complex pathogenesis of CD, which creates an additional challenge in demonstrating clinical efficacy during clinical development

Below mentioned figure illustrates the global sales for CD by region during the 10-year forecast period.

Global CD Sales by Region, 2012–2022



Source: GlobalData

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Research and Development and Corporate Strategies Will Be Focused on the Competitive Biologics Space

- In general, companies striving to enter the CD market appear most focused on patients who are refractory to the first-line anti-TNF biologics, Remicade and Humira. This population remains the most underserved group, with limited therapeutic options and high clinical unmet need. While GlobalData believes this strategy is a viable approach for late-stage CD products, competition within this patient segment is set to intensify from 2014 onwards, following the launch of Takeda's Entyvio and J&J's Stelara. Therefore, companies with early-phase products targeting this patient group may struggle to gain a foothold in the future CD market.
- Indication expansion across autoimmune diseases with biologic brands is another common strategy for companies operating in this therapeutic area. J&J is adept at applying this strategy and appears to be using its leading psoriasis brand, Stelara, an interleukin (IL)-12/23 inhibitor, to address the CD market, while Simponi (golimumab), its biologic brand that is currently approved for other diseases, including rheumatoid arthritis (RA), is targeting the other major type of inflammatory bowel disease (IBD), ulcerative colitis (UC).
- Over the 10-year forecast period, of all the current CD market players, J&J appears to be best positioned to remain a key contender. Although patent expiry looms for its leading brand, Remicade, in 2015 (EU) and 2018 (US), Stelara is forecast to launch in 2015 and will help J&J retain some of its current CD market share, albeit not at the same level as that gained with Remicade. A number of new market players will emerge in the early- to mid-term of the forecast period, and their pipeline drugs are expected to compete against Remicade and AbbVie's Humira. However, they will not be strong enough to displace J&J's current hold on the market. Still, J&J's stance will be weakened, particularly by Takeda, which will play a key role in seizing market share from the biologic brands with Entyvio.
- AbbVie's current leading stance in the CD space is solely attributable to Humira. However, Humira's patent expiries in 2016 (US) and 2018 (EU) will expose the brand to biosimilar competition. With one drug in AbbVie's 2014 CD pipeline, GLPG0634, which is being developed through its collaboration with Galapagos, the ability of Humira to retain sales through strong marketing strategies and tactical pricing in the face of rising biosimilar competition will govern the strength of AbbVie's position at the end of the forecast period. With sales beginning a downward

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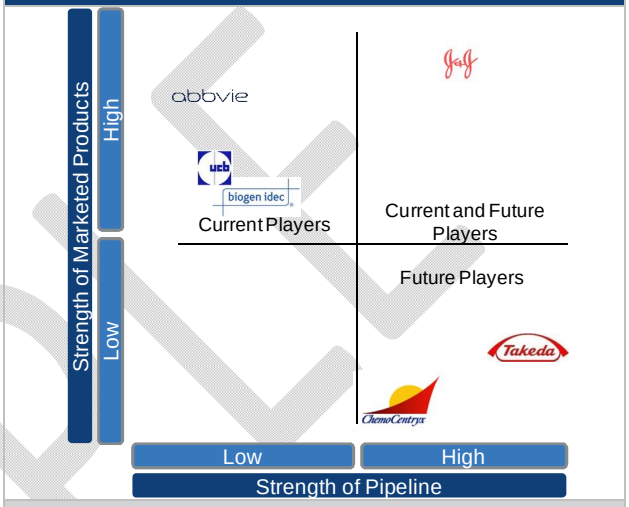
trajectory from 2016 on, Humira will lose almost half its 2012 market value by 2022, thereby dampening AbbVie's CD market status. For UCB and Biogen Idec, their market share and position in CD also will have declined dramatically by 2022, owing to the fact that they are not expected to gain any significant boost in patient share over the forecast period, while the uptake of new products will steer their respective brands, Cimzia (certolizumab pegol) and Tysabri (natalizumab), further down the CD treatment paradigm.

- Although another new market player, ChemoCentryx, will emerge in 2019, with its small-molecule pipeline candidate vercirnon, it will play a less prominent role in the CD market over the forecast period.

Below mentioned figure provides an analysis of the portfolio gap among the companies in the CD market during the forecast period.

Company Portfolio Gap Analysis in CD, 2012–2022



Source: GlobalData

A Number of Clinical Unmet Needs Exist in the CD Treatment Realm

According to key opinion leaders (KOLs) interviewed by GlobalData, the level of unmet need in the CD marketplace is moderate, with clinical unmet needs being the main driver for research into this autoimmune disease. The most pressing clinical unmet need is for reliable disease diagnostic tools, such as biomarkers, as these could aid physicians in predicting the disease course, which would, in turn, allow them to effectively tailor their treatment approach.

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Another significant clinical unmet need lies in the management of patients with moderate to severe CD. These patients eventually lose their response to anti-TNF therapy, which presents a challenge for gastroenterologists, as there are few remaining treatment options. As such, there remains a gap in the market for novel therapies to treat this patient group. Having the most clinically-advanced therapy in targeting this patient group, Takeda appears to be the company best positioned to address this unmet need, and could set a precedent with its novel, gut-selective biologic, Entyvio. The launch of Entyvio into the CD space is imminent, as on December 9, 2013, the Food and Drug Administration's (FDA's) Gastrointestinal Drugs Advisory Committee unanimously voted for its approval as a treatment for adults with moderately to severely active CD.

Focusing on environmental unmet needs, the most pertinent of these is increasing patient awareness of CD, particularly within emerging markets, such as India and China. Improving patient awareness may steer more patients in these markets to seek treatment. This, in turn, would present market expansion opportunities for CD drug developers.

Emerging Therapies Leave Limited Opportunity Within the TNF-Refractory Population

Currently, anti-TNF agents are entrenched in the treatment of CD, but the use of these drugs is associated with the development of immunogenicity. This means that some patients develop infusion site reactions, continue to have active disease, or relapse in spite of biologic therapy. Takeda and J&J are aiming to address the issue of immunogenicity while providing a therapeutic option for anti-TNF refractory patients with their respective biologics, Entyvio and Stelara. With both candidates targeting the anti-TNF refractory patient group and set to enter the CD marketplace by 2015, the need for additional therapies for this population is expected to be met during the coming decade.

The pathophysiology of CD is complex, with a diverse array of possible triggers. This presents several therapeutic targets for drug therapies in CD. Targeting other pathways involved in the cascade that leads to CD, such as the janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, may provide physicians with a greater armamentarium of CD treatments. This presents the opportunity for drug developers to tap into niche segments of the CD population, provide targeted therapy, and circumvent the need for surgery.

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Novel Biologics and Biosimilars Will Reshape the CD Competitive Landscape

Although GlobalData forecasts four new product launches (Entyvio, Stelara, vercirnon, and Prochymal [remestemcel-L]) during the 2012–2022 forecast period, growth within the 10 CD healthcare markets covered in this report will largely be driven by the strong uptake of two of the new products: Takeda's Entyvio and J&J's Stelara. The launch of these pipeline candidates in 2014 and 2015, respectively, in the US, EU, and Canadian markets will boost year-on-year growth from 2014 to 2022 across these major markets, as they will contribute up to $1.0 billion in global CD sales in 2022. This anticipated revenue represents 25% of the overall 2022 global CD market value.

There is palpable excitement among physicians and patients for Entyvio to reach the CD market, owing to the biologic's novel mechanism of action (MOA) as a gut-selective alpha4beta7 integrin inhibitor, its promising Phase III efficacy and safety profile, and its potential to meet the high unmet need for a therapeutic option for patients who are refractory to the established TNF inhibitors, Remicade and Humira. Taking into account the opinions of leading gastroenterologists, the proposed label in Takeda's regulatory documentation for Entyvio, and the clinical trial design of Stelara's Phase III program, both drugs are likely be positioned as second-line biologic agents. This means their primary target population will be anti-TNF failures, placing them in direct competition with Remicade, Humira, Cimzia, and Tysabri.

In addition to the brand dynamics noted above, the launch of biosimilars will contribute to the upward trajectory of the global CD market. Unlike generics of small molecules, which are often priced at a substantial discount to the originator brand, biosimilars of the mAb therapies for CD, Remicade and Humira, are expected to be priced only marginally lower than the biologic brand (at an approximately 20% discount). Although the European Medicines Agency (EMA) has an established pathway for biosimilar approval, which led to the approval of Hospira/Celltrion's Inflectra (infliximab), a biosimilar version of Remicade, in September 2013, the FDA is currently refining its regulatory pathway in this regard. GlobalData assumes that the latter agency will implement guidelines for the approval of biosimilars by the time of Remicade's patent expiry in 2018.

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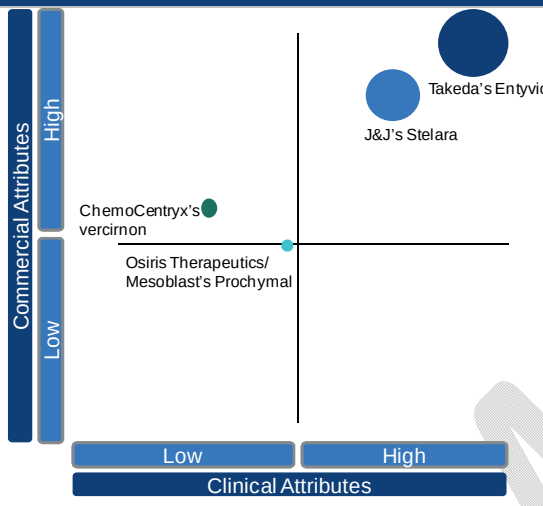
Below mentioned figure provides a competitive assessment of the late-stage pipeline agents in CD during the forecast period.

Competitive Assessment of Late-Stage Pipeline Agents in CD, 2012–2022



Note: Bubble size represents approximate peak year sales of the pipeline drug.

Source: GlobalData

What Do Physicians Think?

Following the approval of Hospira/Celltrion's Inflectra, a biosimilar of the market-leading biologic, Remicade, in September 2013 for the multiple autoimmune indications for which Remicade is approved, some KOLs highlighted that they would await data from a CD- or an IBD-specific trial before prescribing Inflectra for their CD or UC patients. This, in turn, could limit the initial uptake of Inflectra.

"I am not interested in [using] Inflectra in [my] IBD [patients] unless it is tested in IBD[-specific] clinical trials."

[EU] key opinion leader

KOLs stressed that predicting the course of CD remains the most challenging aspect of managing their CD patients.

"I think the most challenging aspect is to, first of all, risk-stratify as to what patients are going to do badly in the long run, and trying to tailor an effective therapy for them."

[Outside-US] key opinion leader

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Having biomarkers included in their diagnostic tools is important to gastroenterologists, as it could allow them to effectively predict the course of CD in a given patient and allow them to offer a personalized treatment approach.

"I think we need a more biomarker-based approach….I think we are falsely diagnosing early disease. With Crohn's, two days of endoscopic techniques and two days of radiological assessments are precise enough to allow you to see the morphological damage, but in pre-stage patients at risk of developing the disease, we do have difficulties in properly assessing the disease."

[EU] key opinion leader

KOLs stressed their desire for new drug therapies to treat the anti-TNF refractory patient segment.

"We are learning that the anti-TNF therapies have a limited lifespan….We are going to run into a problem where we have a lot of people losing response to anti-TNF therapy early on in their disease course, and then they don't have an option later on."

[US] key opinion leader

"All these drugs [anti-TNFs] have a finite natural history, as we rapidly move from one drug to another, and five years down the road, someone with a history of Crohn's is going to be with no treatment options."

[US] key opinion leader

KOLs validated that emerging therapies with novel MOAs will form the basis of their treatment paradigm.

"In the future, what we will do is either switching of anti-TNF therapies, or we will switch to alternative mechanisms, and we will soon have [the] alpha4beta7, vedolizumab."

[EU] key opinion leader

According to KOLs, anti-IL-6 therapies, which are currently in early clinical development, hold promise.

"There are so many companies out there with anti-IL-6 agents that I feel there could be a new paradigm coming up, which could add to the value of innovation…not just to the molecule, but also to the way we use it."

[EU] key opinion leader

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2 Introduction

2.1 Catalyst

The Crohn's disease (CD) market is currently very dynamic, with novel biologic therapies on the horizon, such as:

- Takeda's alpha4beta7 inhibitor, Entyvio (vedolizumab)
- Johnson & Johnson's (J&J's) interleukin (IL)-12/23 inhibitor, Stelara (ustekinumab)

These compounds will challenge the current biologics in an attempt to dislodge the stronghold of the TNF inhibitors, as they aim to tap into the lucrative portion of the CD therapeutics market. If their promising safety and efficacy profiles translate to clinical practice once they enter the market, their launch will be to the detriment of the existing market leaders, Remicade (infliximab) and Humira (adalimumab).

The loss of patent protection of the anti-TNF marketed brands will allow for the emergence of biosimilars, such as Hospira's Inflectra (infliximab) a Remicade biosimilar. Patent expiries begin in 2015 for the current market leaders:

- J&J's Remicade
- AbbVie's Humira

Focusing on country dynamics, Canada and the emerging markets of China and India will also play a key role in driving growth in the long term, with each market forecast to post positive Compound Annual Growth Rates (CAGRs) from 2012 to 2022, primarily due to the anticipated strong uptake of Remicade over the forecast period.

Exciting times lay ahead for the CD marketplace, as the market events noted above are due to occur against the backdrop of a steadily rising global CD prevalent population. With the clinical unmet need for better diagnostic tools and treatment options for the anti-TNF-refractory population, CD represents an attractive autoimmune disease for drug developers. This, in turn should fuel commercial interest in this subtype of IBD.

Introduction

2.2 Related Reports

- GlobalData (2013). PharmaPoint: Psoriasis – Global Drug Forecast and Market Analysis to 2022, May 2013, GDHC48PIDR
- GlobalData (2013). PharmaPoint: Rheumatoid Arthritis – Global Drug Forecast and Market Analysis Event-Driven Update, July 2013, GDHC60PIDR

2.3 Upcoming Related Reports

- GlobalData (2014). PharmaPoint: Ulcerative Colitis – Global Drug Forecast and Market Analysis to 2022

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.

11.9 Disclaimer