Sales for Ulcerative Colitis in the United States

In 2012, GlobalData estimated that the US Ulcerative Colitis (UC) market reached $2.25 billion. By the end of the forecast period, in 2022, sales across the US will grow steadily to reach $3.49 billion, representing a Compound Annual Growth Rate (CAGR) of 4.5% over the 10-year timeframe, which includes four new market entrants and the launch of biosimilars.

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

- Higher uptake of existing biologic drugs and the launch of new biologics
- Affordable Care Act (ACA)
- Eventual introduction of a biosimilar regulatory pathway

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

- Pricing pressures due to US healthcare reform
- Insurance challenges and the affordability of expensive biologic therapies
- High lack of compliance

Figure below illustrates the US Ulcerative Colitis sales during the 10-year forecast period.
Executive Summary

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
Table of Contents

1 Table of Contents

1.1 List of Tables ...................................................................................................................... 8

1.2 List of Figures ................................................................................................................... 10

2 Introduction ............................................................................................................................... 11

2.1 Catalyst ............................................................................................................................. 11

2.2 Related Reports ................................................................................................................ 11

2.3 Upcoming Related Reports ............................................................................................... 13

3 Disease Overview ..................................................................................................................... 14

3.1 Etiology and Pathophysiology ........................................................................................... 14

3.1.1 Etiology ......................................................................................................................... 14

3.1.2 Pathophysiology ............................................................................................................ 17

3.2 Symptoms ......................................................................................................................... 18

3.2.1 Quality of Life ................................................................................................................ 19

4 Disease Management ............................................................................................................... 20

4.1 Diagnosis and Treatment Overview .................................................................................. 20

4.1.1 Diagnosis ...................................................................................................................... 20

4.1.2 Treatment Guidelines and Leading Prescribed Drugs ................................................... 24

4.1.3 Clinical Practice ............................................................................................................. 25

4.2 US..................................................................................................................................... 29

5 Competitive Assessment .......................................................................................................... 32

5.1 Overview ........................................................................................................................... 32

5.2 Strategic Competitor Assessment ..................................................................................... 33

5.3 Product Profiles – Major Brands ....................................................................................... 35

5.3.1 Remicade (infliximab) .................................................................................................... 35

5.3.2 Humira (adalimumab) .................................................................................................... 42

5.3.3 Simponi (golimumab) .................................................................................................... 47
## Table of Contents

5.3.4 Apriso (mesalamine) ..................................................................................................... 50
5.3.5 Asacol HD (mesalamine) ............................................................................................... 55
5.3.6 Lialda (mesalamine) ...................................................................................................... 59
5.3.7 Pentasa (mesalamine) .................................................................................................. 62
5.3.8 Colazal (balsazide disodium) ........................................................................................ 65
5.3.9 Giazo (balsalazide disodium) ........................................................................................ 68
5.3.10 sfRowasa (mesalamine) ................................................................................................ 71
5.3.11 Uceris (budesonide) ...................................................................................................... 73
5.3.12 Other Drug Classes Used in the Treatment of UC ......................................................... 76
5.4 Biosimilars ........................................................................................................................ 77
5.4.1 Introduction ................................................................................................................... 77
5.4.2 Hospira’s Inflectra Versus J&J’s Remicade in Key Autoimmune Diseases .................... 78
5.4.3 Biosimilars in the Immunology Community .................................................................. 78
5.4.4 By the Numbers: Biosimilars in Development ................................................................. 79
5.4.5 The Impact of Biosimilars Will be Felt Throughout the Pharmaceutical Industry ............ 81
6 Opportunity and Unmet Need ........................................................................................... 83
6.1 Overview ........................................................................................................................... 83
6.2 Unmet Needs .................................................................................................................... 84
6.2.1 Curative Therapy for Severe UC Patients ...................................................................... 84
6.2.2 Diagnostic Markers for Disease Severity ..................................................................... 84
6.2.3 Personalized Therapy ................................................................................................... 85
6.2.4 A Replacement for Steroids ........................................................................................... 85
6.2.5 Novel Oral Drug Formulations ....................................................................................... 86
6.2.6 Preventative Medicine for Lowering the Associated Colorectal Cancer Risk ................. 87
6.2.7 Improved Management of Infectious Adverse Events .................................................... 87
6.3 Unmet Needs Gap Analysis ............................................................................................. 88
6.4 Disease Severity and Colorectal Cancer Biomarker-Based Prognostic Tools .................... 89
# Table of Contents

6.5  Predictors of Medically-Refractory Disease ................................................................. 90

7  Pipeline Assessment ............................................................................................................ 91
   7.1  Overview .......................................................................................................................... 91
   7.2  Promising Drugs in Clinical Development ................................................................. 91
       7.2.1  Entyvio (vedolizumab) ............................................................................................. 93
       7.2.2  Xeljanz (tofacitinib) ............................................................................................... 102

8  Market Outlook .................................................................................................................. 108
   8.1  United States ................................................................................................................. 108
       8.1.1  Forecast .................................................................................................................... 108
       8.1.2  Key Events ............................................................................................................. 113
       8.1.3  Drivers and Barriers .............................................................................................. 113

9  Appendix ............................................................................................................................ 116
   9.1  Bibliography .................................................................................................................. 116
   9.2  Abbreviations ................................................................................................................. 120
   9.3  Methodology ................................................................................................................... 124
       9.4  Forecasting Methodology .......................................................................................... 124
           9.4.1  Diagnosed UC Patients ....................................................................................... 124
           9.4.2  Percent Drug-Treated Patients ............................................................................. 125
           9.4.3  Drugs Included in Each Therapeutic Class .......................................................... 125
           9.4.4  Launch and Patent Expiry Dates .......................................................................... 125
           9.4.5  General Pricing Assumptions .............................................................................. 126
           9.4.6  Individual Drug Assumptions .............................................................................. 126
           9.4.7  Generic Erosion .................................................................................................. 128
           9.4.8  Pricing of Pipeline Agents .................................................................................... 128
   9.5  Physicians and Specialists Included in This Study ....................................................... 129
   9.6  Primary Research – Prescriber Survey ....................................................................... 131
   9.7  About the Authors ........................................................................................................ 132
Table of Contents

9.7.1 Author ......................................................................................................................... 132
9.7.2 Global Head of Healthcare .......................................................................................... 133
9.8 About GlobalData............................................................................................................ 134
9.9 Disclaimer ....................................................................................................................... 134

1.1 List of Tables
Table 1: Genetic Factors That Confer a Predisposition to UC .............................................. 16
Table 2: Typical Symptoms of UC ....................................................................................... 18
Table 3: Truelove and Witts UC Severity Index ....................................................................... 22
Table 4: UCDAI ..................................................................................................................... 23
Table 5: Treatment Guidelines for UC Used in the 10MM ................................................... 24
Table 6: Most Commonly Prescribed Drugs for UC by Class in the 10MM, 2013 .................. 25
Table 7: UC Management Country Profile – US .................................................................... 31
Table 8: Leading Treatments for UC, 2014 .......................................................................... 34
Table 9: Product Profile – Remicade ..................................................................................... 37
Table 10: Remicade SWOT Analysis, 2014 ......................................................................... 41
Table 11: Product Profile – Humira ...................................................................................... 43
Table 12: Humira Efficacy in the ULTRA 2 Trial ................................................................. 44
Table 13: Product Efficacy Comparison – Humira vs. Remicade ............................................ 44
Table 14: Humira SWOT Analysis, 2014 ............................................................................. 46
Table 15: Product Profile – Simponi ...................................................................................... 48
Table 16: Simponi SWOT Analysis, 2014 ............................................................................ 50
Table 17: Product Profile – Apriso ....................................................................................... 52
Table 18: Apriso SWOT Analysis, 2014 .............................................................................. 54
Table 19: Product Profile – Asacol HD ................................................................................ 56
# Table of Contents

Table 20: Asacol HD SWOT Analysis, 2014 ................................................................. 59  
Table 21: Product Profile – Lialda ........................................................................ 60  
Table 22: Lialda SWOT Analysis, 2014 ................................................................. 62  
Table 23: Product Profile – Pentasa ........................................................................ 63  
Table 24: Pentasa SWOT Analysis, 2014 ............................................................. 65  
Table 25: Product Profile – Colazal ....................................................................... 66  
Table 26: Colazal SWOT Analysis, 2014 .............................................................. 68  
Table 27: Product Profile – Giazo .......................................................................... 69  
Table 28: Giazo SWOT Analysis, 2014 ................................................................. 71  
Table 29: Product Profile – sfRowasa .................................................................... 72  
Table 30: sfRowasa SWOT Analysis, 2014 .......................................................... 73  
Table 31: Product Profile – Uceris ......................................................................... 74  
Table 32: Uceris SWOT Analysis, 2014 ............................................................... 76  
Table 33: Summary of Other Immunomodulators for UC, 2013 ......................... 77  
Table 34: Biosimilars Pipeline, 2013 ..................................................................... 80  
Table 35: Overall Unmet Needs – Current Level of Attainment ......................... 83  
Table 36: Corticosteroid Long-Term Side Effects ............................................... 86  
Table 37: Clinical Unmet Needs in UC – Gap Analysis, 2013 ............................. 89  
Table 38: Prognostic Markers in UC ................................................................. 90  
Table 39: UC – Pre-Registration and Phase III Pipeline, 2014 ............................ 91  
Table 40: Comparison of Therapeutic Classes in Development for UC, 2014 .......................... 92  
Table 41: Product Profile – Entyvio ...................................................................... 95  
Table 42: Results of the GEMINI I Trial, Efficacy of Vedolizumab in the Induction of Remission in UC ....... 96  
Table 43: Results of the GEMINI I Trial, Efficacy of Vedolizumab in the Maintenance of Remission in UC ...... 97
Table of Contents

Table 44: Most Common Adverse Events with Vedolizumab in the GEMINI I Study........................................ 98
Table 45: Entyvio SWOT Analysis, 2014......................................................................................................... 101
Table 46: Product Profile – Xeljanz.............................................................................................................. 102
Table 47: Results of Phase IIa Trial of Xeljanz in the Induction of Remission in UC.................................... 103
Table 48: Most Common Adverse Events in the Phase IIa Trial of Xeljanz.................................................. 105
Table 49: Xeljanz SWOT Analysis, 2014......................................................................................................... 107
Table 50: Sales Forecasts ($m) for UC in the US, 2012–2022................................................................. 110
Table 51: Key Events Impacting Sales for UC in the US, 2012–2022......................................................... 113
Table 52: UC Market in the US – Drivers and Barriers, 2012–2022......................................................... 113
Table 53: Key launches for Ulcerative Colitis, 2012-2022........................................................................ 125
Table 54: Key Patent Expiries....................................................................................................................... 126
Table 55: Annual Cost of Therapy for 5-ASAs ($)..................................................................................... 128
Table 56: Physicians Surveyed, By Country.................................................................................................. 131

1.2 List of Figures

Figure 1: Cellular Mechanisms Involved in the Pathogenesis of UC ......................................................... 18
Figure 2: UC Disease Management Flowchart.......................................................................................... 28
Figure 3: Competitive Assessment of Late-Stage Pipeline Agents UC, 2012–2022............................... 92
Figure 4: Sales for UC in the US by Drug Class, 2012–2022.................................................................... 112
Introduction

2 Introduction

2.1 Catalyst

The catalysts for this report are to:

- 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.
- Examine the impact that Entyvio’s (vedolizumab’s) estimated launch in 2014 will have on the management of ulcerative colitis (UC) and the competitive landscape in terms of market value.
- 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

- GlobalData (2014). Entyvio (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC342DFR
- GlobalData (2014). Xeljanz (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC343DFR
- GlobalData (2014). Kappaproct (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC344DFR
- GlobalData (2014). Remicade (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC345DFR
- GlobalData (2014). Humira (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC346DFR
- GlobalData (2014). Simponi (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC347DFR
- GlobalData (2014). Apriso (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC348DFR
- GlobalData (2014). Asacol HD (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC349DFR
- GlobalData (2014). Lialda (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC350DFR
Introduction

- GlobalData (2014). Pentasa (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC351DFR
- GlobalData (2014). Colazal & Giazo (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC352DFR
- GlobalData (2014). sfRowasa (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC353DFR
- GlobalData (2014). Uceris (Ulcerative Colitis) – Forecast and Market Analysis to 2022, February 2014, GDHC354DFR

2.3 Upcoming Related Reports

9.8 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.

9.9 Disclaimer

All Rights Reserved.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior permission of the publisher, GlobalData.