ATOPIC DERMATITIS – SPAIN DRUG FORECAST AND MARKET ANALYSIS TO 2022
Executive Summary

Sales for Atopic Dermatitis in the Spain

The Spain Atopic Dermatitis market was worth approximately $148.12 million in 2012, with a projected compound annual growth rate (CAGR) of 5.24%, to reach a total of $246.83 million in 2022.

Major growth drivers in the atopic dermatitis market over the forecast period include:

- Launch of the first biologic mid-forecast may alter the moderate-to-severe atopic dermatitis treatment landscape.

Conversely, major barriers to the growth of the atopic dermatitis market include:

- Stringent pricing policies that are in place for innovative drugs present a hurdle for novel, expensive therapies hoping to penetrate Spain’s atopic dermatitis market.

The figure below illustrates the Spain atopic dermatitis sales by region during the 10-year forecast period.

![Graph showing Spain atopic dermatitis sales by region from 2012 to 2022](source: GlobalData)
Executive Summary

What Do the Physicians Think?

Key opinion leaders highlight that atopic dermatitis patients remain dissatisfied with the efficacy and side-effect profiles of currently available treatments.

“I am not convinced that anything [in terms of therapies] that we have now that we can go to is acceptable to a lot of people...because people also come to us [specialists] because they are not happy with the therapy they are getting [from their PCPs] and they just want to know if there is some way of using an approach that may not be harmful in terms of adverse events.”

[US] key opinion leader, May 2013

Opinion leaders highlight that there remains substantial research to be carried out to further understand the pathophysiology of atopic dermatitis, and that existing therapies cannot be used to treat all patients:

“Probably at least for each subset [of atopic dermatitis patient]; because there probably could be easily five types of AD, if not 10 [types] and so trying to [treat] everyone under the same umbrella does not work.”

[US] key opinion leader, May 2013

Leading dermatologists interviewed by GlobalData highlighted the challenges drug developers of potential atopic dermatitis treatments face. This ranges from high drug attrition due to the complex pathophysiology of atopic dermatitis, and the high pediatric population, to past actions by the US Food and Drug Administration (FDA) which may have hampered innovation:

“[In terms of drug attrition in atopic dermatitis], the problem is the target [i.e., the disease itself], and the second major problem is that the majority of patients are in the pediatric population. [Therefore], for a small company, which is sitting on the license of a new product or compound and is trying to sell it, and then trying to have some clinical evidence that their product is a good business [strategy] for one of the big Pharma companies, they usually have a really hard time to provide something which is convincing. [This is] because it is so cumbersome to be able to really provide the data in this particular pediatric patient population. Meanwhile, the regulatory framework is so rigid and so difficult and safety is [a major concern for the pediatric group] that most of the companies are in fact stopping the development of their [atopic dermatitis pipeline] product. [That is] even if they have some positive signals, they still have to stop because they cannot find the investors or enough money to continue the clinical program. That is the typical valley of death phenomenon that we see in drug development [for atopic dermatitis].”

[EU] key opinion leader, May 2013
Executive Summary

“Unfortunately, the FDA stuck a black box on [Protopic and Elidel] many years ago, which was unwarranted, [and] has never proved [to be an issue with these therapies]... It was a theoretical reason and it has never shown over the last 12 years to be a problem. But the FDA never removes black boxes so it is stuck there, and it has been another reason why we cannot get [calcineurin inhibitors] very easily for patients. A lot of dermatologists do not even bother trying to, because it is so much of a hassle and it takes so much time for doctors and staff.”

[US] key opinion leader, September 2013

“The initial release of the calcineurin inhibitors [Protopic and Elidel] lead to the black box [warning on their labels], and the black box was more a reflection of the lack of knowledge regarding long-term side effects. I think that now that they are 10 years out from [their first] release [i.e., launch] there could be more use of them because they really have not caused the skin cancer that the FDA was concerned about. I think the [greater] problem [with the calcineurin inhibitors] is cost. Most patients would be happy to use them but because the major manufacturers have abandoned these [products] their cost is great and a lot of patients do not have it covered under their insurance.”

[US] key opinion leader, May 2013

GlobalData identified palpable excitement over the late-stage therapies in the atopic dermatitis pipeline and the potential hope they bring for the pediatric atopic dermatitis population:

“It is just so exciting to finally have some new drugs and I hope that they are tested and approved for children. Because children unfortunately do not get a lot of these drugs easily and it becomes hard without the [clinical trial] testing to be able to utilize them [in this patient group]. It is the school age or above who need this type of therapy with respect to the systemic [dupilumab], for the new PDE4 inhibitor [AN2728] that would be great if the toxicity testing was good so that we would be able to use it for younger children.”

[US] key opinion leader, September 2013
Table of Contents

1 Table of Contents .......................................................................................................................... 5

1.1 List of Tables .......................................................................................................................... 9

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

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

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

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

2.3 Upcoming Related Reports ................................................................................................... 12

3 Disease Overview ....................................................................................................................... 13

3.1 Etiology and Pathophysiology ............................................................................................... 13

3.1.1 Etiology ........................................................................................................................... 13

3.1.2 Pathophysiology ............................................................................................................. 14

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

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

4.1 Diagnosis ............................................................................................................................. 20

4.2 Treatment Overview ............................................................................................................. 22

4.3 Spain .................................................................................................................................... 28

4.3.1 Diagnosis ........................................................................................................................ 28

4.3.2 Clinical Practice .............................................................................................................. 29

5 Competitive Assessment ............................................................................................................. 31

5.1 Overview ............................................................................................................................... 31

5.2 Strategic Competitor Assessment ......................................................................................... 32
# Table of Contents

5.3 Product Profiles – Major Brands ........................................................................................................... 33
  5.3.1 Protopic (tacrolimus) .................................................................................................................. 33
  5.3.2 Elidel ............................................................................................................................................ 40
  5.3.3 Cyclosporine (numerous generic names) .................................................................................... 46
  5.3.4 Other Therapeutic Drug Classes Used in Atopic Dermatitis .................................................... 49

6 Opportunity and Unmet Need .................................................................................................................. 51
  6.1 Overview .......................................................................................................................................... 51
  6.2 Unmet Needs ..................................................................................................................................... 52
    6.2.1 A Systemic Drug for Severe Recalcitrant Patients .................................................................... 52
    6.2.2 Tests that Stratify Patients and Allow for a Tailored Treatment Approach ............................. 54
    6.2.3 A Drug that Effectively Controls Patients’ Pruritus .................................................................. 55
    6.2.4 Further Research into the Pathophysiology of Atopic Dermatitis ......................................... 56
    6.2.5 A Drug that Induces Disease Remission .................................................................................. 57
    6.2.6 Improved Quality of Life for Both Patients and their Carers .................................................. 58
  6.3 Unmet Needs Gap Analysis .............................................................................................................. 58
  6.4 Opportunities .................................................................................................................................... 60
    6.4.1 Increase Treatment Armamentarium for Severe Recalcitrant Patients ................................. 60
    6.4.2 Predictive Tests for Patient Stratification .................................................................................. 60
    6.4.3 More Therapeutic Options that Address Patients’ Pruritus .................................................... 61

7 Pipeline Assessment ................................................................................................................................ 62
  7.1 Overview .......................................................................................................................................... 62
  7.2 Promising Drugs in Clinical Development ....................................................................................... 63
    7.2.1 Dupilumab (SAR231893/ REGN668) ..................................................................................... 65
Table of Contents

7.2.2 Phase II Pipeline Products ........................................................................................................... 74

8 Market Outlook ...................................................................................................................................... 76

8.1 Global Drivers and Barriers ........................................................................................................... 76

8.1.1 Driver: Anticipated launch of the first biologic for the treatment of moderate to severe disease .......................................................................................................................... 76

8.1.2 Driver: The underserved severe refractory patient segment presents an untapped market opportunity ......................................................................................................................................... 77

8.1.3 Driver: A drug that is able to target two or more atopic diseases would gain a foothold in these markets .................................................................................................................................. 77

8.1.4 Driver: Atopic dermatitis presents an attractive patient population for drug developers ... 77

8.1.5 Driver: Restoring skin barrier function remains a key goal of disease management, meaning a continued need for moisturizers and topical agents .................................................................................. 78

8.1.6 Barrier: First to second line of therapy is dominated by cheap, genericized topical drugs which create significant obstacles for novel drugs hoping to penetrate the market........ 79

8.1.7 Barrier: The largest atopic dermatitis patient segment – mild disease – can be well-controlled on most forms of topical therapy ........................................................................................................... 79

8.1.8 Barrier: Pediatric sufferers are the largest patient group and pose a high bar in terms of safety for new products .................................................................................................................................. 79

8.1.9 Barrier: The complexity of the multiple etiologies that lead to atopic dermatitis means that treatment outcomes with existing drugs are not universal across all patient groups ...... 80

8.1.10 Barrier: A significant proportion of patients experience disease remission in their early adolescent years and this may occur without drug therapy ...................................................... 81

8.2 Spain ................................................................................................................................................. 81

8.2.1 Forecast ....................................................................................................................................... 81

8.2.2 Key Events .................................................................................................................................... 84
# Table of Contents

8.2.3 Drivers and Barriers ........................................................................................................ 85

9 Appendix ..................................................................................................................................... 87

9.1 Bibliography .......................................................................................................................... 87

9.2 Abbreviations ........................................................................................................................ 92

9.3 Methodology ......................................................................................................................... 93

9.4 Forecasting Methodology ..................................................................................................... 94

9.4.1 Diagnosed Atopic Dermatitis Patients ............................................................................. 94

9.4.2 Percent Drug-treated Patients ......................................................................................... 94

9.4.3 Drugs Included in Each Therapeutic Class ..................................................................... 95

9.4.4 Launch and Patent Expiry Dates ..................................................................................... 95

9.4.5 General Pricing Assumptions .......................................................................................... 95

9.4.6 Individual Drug Assumptions .......................................................................................... 97

9.4.7 Generic Erosion .............................................................................................................. 98

9.4.8 Pricing of Pipeline Agents ............................................................................................... 99

9.5 Physicians and Specialists Included in this Study ............................................................... 100

9.6 Primary Research – Prescriber Survey ............................................................................... 101

9.7 About the Authors ............................................................................................................... 102

9.7.1 Author ........................................................................................................................... 102

9.7.2 Global Head of Healthcare ............................................................................................ 103

9.8 About GlobalData ............................................................................................................... 104

9.9 Disclaimer ............................................................................................................................ 104
# Table of Contents

## 1.1 List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Symptoms of Atopic Dermatitis</td>
<td>19</td>
</tr>
<tr>
<td>Table 2</td>
<td>Treatment Guidelines for Atopic Dermatitis</td>
<td>25</td>
</tr>
<tr>
<td>Table 3</td>
<td>Most Prescribed Drugs for Atopic Dermatitis by Severity in the Global Markets, 2013</td>
<td>27</td>
</tr>
<tr>
<td>Table 4</td>
<td>Referral Rates to a Spanish Dermatologist, Split by Severity and Specialist Type, 2013</td>
<td>28</td>
</tr>
<tr>
<td>Table 5</td>
<td>Key Metrics Relating to the Diagnosis, Relapse and Remission Rates of Atopic Dermatitis in Spain in 2012</td>
<td>29</td>
</tr>
<tr>
<td>Table 6</td>
<td>Leading Treatments for Atopic Dermatitis, 2013</td>
<td>33</td>
</tr>
<tr>
<td>Table 7</td>
<td>Product Profile – Protopic</td>
<td>35</td>
</tr>
<tr>
<td>Table 8</td>
<td>Clinical Response Data of Protopic (0.03% and 0.1%) versus Vehicle Ointment at Week 12 from One Study in Pediatric Patients and Two Combined Studies in Adult Patients</td>
<td>36</td>
</tr>
<tr>
<td>Table 9</td>
<td>Protopic SWOT Analysis, 2013</td>
<td>39</td>
</tr>
<tr>
<td>Table 10</td>
<td>Product Profile – Elidel</td>
<td>41</td>
</tr>
<tr>
<td>Table 11</td>
<td>Combined Clinical Efficacy Results of Elidel versus Vehicle Cream at Week 6 from Two Phase III Studies</td>
<td>42</td>
</tr>
<tr>
<td>Table 12</td>
<td>Elidel SWOT Analysis, 2013</td>
<td>45</td>
</tr>
<tr>
<td>Table 13</td>
<td>Product Profile – Cyclosporine</td>
<td>47</td>
</tr>
<tr>
<td>Table 14</td>
<td>Cyclosporine SWOT Analysis, 2013</td>
<td>49</td>
</tr>
<tr>
<td>Table 15</td>
<td>Summary of Other Therapeutic Classes for Atopic Dermatitis, 2013</td>
<td>50</td>
</tr>
<tr>
<td>Table 16</td>
<td>Overall Unmet Needs in Atopic Dermatitis – Current Level of Attainment</td>
<td>52</td>
</tr>
<tr>
<td>Table 17</td>
<td>Clinical Unmet Needs in Atopic Dermatitis – Gap Analysis, 2013</td>
<td>59</td>
</tr>
<tr>
<td>Table 18</td>
<td>Late-Stage Atopic Dermatitis Pipeline, 2013</td>
<td>63</td>
</tr>
<tr>
<td>Table 19</td>
<td>Comparison of Therapeutic Classes in Development for Atopic Dermatitis, 2013</td>
<td>65</td>
</tr>
<tr>
<td>Table 20</td>
<td>Product Profile – Dupilumab</td>
<td>67</td>
</tr>
<tr>
<td>Table 21</td>
<td>Ongoing Clinical Trials of Dupilumab in Atopic Dermatitis Patients, as of September 2013</td>
<td>69</td>
</tr>
<tr>
<td>Table 22</td>
<td>Dupilumab SWOT Analysis, 2013</td>
<td>74</td>
</tr>
</tbody>
</table>
Table of Contents

Table 23: Phase II and Phase I Atopic Dermatitis Pipeline, 2013 .................................................. 74
Table 24: Global Atopic Dermatitis Market – Drivers and Barriers, 2012–2022 .................................. 76
Table 25: Sales Forecasts ($m) for Atopic Dermatitis in Spain, 2012–2022 ........................................ 83
Table 26: Key Event Impacting Sales for Atopic Dermatitis in Spain, 2012–2022 ............................. 84
Table 27: Atopic Dermatitis Market in Spain – Drivers and Barriers, 2012–2022 ............................. 85
Table 28: Key Launch Dates .............................................................................................................. 95
Table 29: Key Patent Expiries ........................................................................................................... 95
Table 30: Physicians Surveyed, By Country ..................................................................................... 101

1.2 List of Figures

Figure 1: Immunologic Pathway Involved in Healthy, Acute Atopic Dermatitis, and Chronic Atopic
Dermatitis Skin ................................................................................................................................. 16

Figure 2: Flow Chart of the Diagnosis and Management of Atopic Dermatitis ................................. 23

Figure 3: Competitive Assessment of Late-Stage Pipeline Agents in Atopic Dermatitis, 2012–2022 ... 64

Figure 4: Sales for Atopic Dermatitis in Spain by Drug Class, 2012–2022 ......................................... 84
2 Introduction

2.1 Catalyst

Although the past decade has seen the atopic dermatitis market remain relatively unchanged and a saturated, highly genericized arena, the coming decade could see the launch of the first biologic, which will set a precedent and pave the way for others to follow suit.

By the mid-to-late term of GlobalData’s 2012 to 2022 forecast, Sanofi/Regeneron’s pipeline biologic dupilumab is expected to reshape the moderate and severe treatment landscape.

Other events that are expected to invoke change to the previously stagnant atopic dermatitis market include the launch of a non-steroidal topical from Anacor, AN2728, generic erosion of branded topicals Protopic and Elidel in the US, and the increasing use of pharmacological treatments in the growing markets of India and China.

Exciting times lay ahead for the atopic dermatitis market place; as the above events are due to occur against the backdrop of increasing research into the multiple etiologies that give rise to the disease. With existing unmet need for a better treatment armamentarium for severe, refractory/recalcitrant disease and an estimated drug-treated population that hovers around the 54 million mark over the next decade, atopic dermatitis represents an attractive dermatology sector for drug developers, and this in turn should fuel commercial interest into this marketplace.

2.2 Related Reports

Introduction

- GlobalData (2013). Atopic Dermatitis - Germany Drug Forecast and Market Analysis to 2022, November 2013, GDHC185CFR
- GlobalData (2013). Atopic Dermatitis - Italy Drug Forecast and Market Analysis to 2022, November 2013, GDHC186CFR
- GlobalData (2013). Atopic Dermatitis - UK Drug Forecast and Market Analysis to 2022, November 2013, GDHC188CFR
- GlobalData (2013). Atopic Dermatitis - India Drug Forecast and Market Analysis to 2022, November 2013, GDHC191CFR
- GlobalData (2013). Protopic (Atopic Dermatitis) - Forecast and Market Analysis to 2022, November 2013, GDHC294DFR.
- GlobalData (2013). Elidel (Atopic Dermatitis) - Forecast and Market Analysis to 2022, November 2013, GDHC295DFR.
- GlobalData (2013). Dupilumab (Atopic Dermatitis) - Forecast and Market Analysis to 2022, November 2013, GDHC296DFR.
- GlobalData (2013). AN2728 (Atopic Dermatitis) - Forecast and Market Analysis to 2022, November 2013, GDHC297DFR
- GlobalData (2013). Atopic Dermatitis - Current and Future Players. GDHC1024FPR

2.3 Upcoming Related Reports

Appendix

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, Boston, London, India and Singapore.

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.