Executive Summary

Below mentioned table presents the key metrics for diabetic foot ulcers (DFUs) in the six major pharmaceutical markets covered in this report (US, France, Germany, Italy, Spain, and UK) during the forecast period from 2012–2017.

### Diabetic Foot Ulcers (DFUs): Key Metrics in the Six Major Markets (6MM)*

<table>
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<tr>
<td>2012 Market Sales</td>
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<td>5EU</td>
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<td>Number of first-in-class drugs</td>
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<td>Key Events (2012–2017)</td>
<td>Level of Impact</td>
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<td>Launch of Cogenzia (gentamicin-collagen sponge) in the US in 2015; EU markets in 2016</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Launch of trafermin in the EU in 2015 and 2016</td>
<td>↑↑</td>
</tr>
<tr>
<td>Launch of Locilex (pexiganan acetate cream 1%) in the US in 2016; EU in 2017</td>
<td>↑</td>
</tr>
<tr>
<td>Launch of DSC127 in the US in 2017</td>
<td>↑↑</td>
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<tr>
<td>Launch of CureXcell (activated leukocyte suspension) in the US in 2017</td>
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<tr>
<td>2017 Epidemiology</td>
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<tr>
<td>2017 Market Sales</td>
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<tr>
<td>5EU</td>
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<tr>
<td>Total</td>
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Source: GlobalData

*RFor the purposes of this report, the 6MM = US and 5EU (France, Germany, Italy, Spain, and UK)

**Rapid Growth in the Diabetic Foot Ulcer Market is Expected from 2012 to 2017**

GlobalData estimates the 2012 sales for DFUs at approximately $302m across the six major pharmaceutical markets covered in this report: the US, France, Germany, Italy, Spain, and the UK. The US contributed the majority of these sales, generating an estimated $238m. By the end of the forecast period in 2017, DFU sales are forecast to grow to $1.58 billion at a Compound Annual Growth Rate (CAGR) of 39.3% over the five-year period. The majority of sales will come from the US, which will represent 85% of the market (based on the 6MM) in 2017.

Major drivers of the growth of the DFU market over the forecast period will include:

- The introduction of several novel wound-healing agents, which are administrated as a topical ointment or spray, or are injected directly into the wound bed: Macro cure’s CureXcell, Derma Sciences’ DSC127, and Olympus Biotech’s trafermin.
- The launch of the first topical antibacterials indicated specifically for the treatment of diabetic foot infections, which will be used as an adjunct to systemic antibiotic therapy, or to treat mild infections: Innocoll’s Cogenzia and Dipexium Pharmaceuticals’ Locilex.
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- Increased emphasis on the cost-effectiveness of advanced DFU treatments in preventing serious complications, including infection, amputation, and death.

- The growing number of patients suffering from a DFU due to an overall increase in the prevalence of diabetes across all the markets.

Major barriers to the growth of the DFU market will include:

- Anticipated high prices for the wound-healing agents currently in development, which developers can justify due to the high level of unmet need for treatments for DFUs. High prices may prevent reimbursement by local health authorities and health insurance companies.

- Physician familiarity with widely-used systemic antibiotics may inhibit the uptake of novel topical antibacterials. Oral antibiotics may also be considered to be more convenient than topical products, and concerns related to patient compliance with topical therapies may limit prescribing.

- A lack of evidence-based clinical efficacy data may inhibit the uptake of novel DFU treatments. Key opinion leaders (KOLs) believe that more well-designed clinical trials must be performed to demonstrate that advanced wound-care products are superior to the current standard of care.

Below mentioned figure illustrates the DFU sales for the US and the five major EU (5EU) markets during the forecast period.

![DFU Sales by Region, 2012–2017](image)

**Companies Employ Diverse Research and Development Strategies to Gain Entry Into the DFU Market**

While various treatment modalities are available for the management of DFUs, Smith & Nephew's Regranex (becaplermin) is currently the only marketed pharmaceutical-based wound-healing agent for the treatment of this indication. Regranex’s limited uptake due to its perceived lack of efficacy has left an untapped market in the pharmaceutical arena. Research and development (R&D) strategies for wound-healing agents for the treatment of DFUs are very diverse and range from the development of locally-administered growth factors and bioactive peptides to living cell-based therapies. With different treatment modalities...
Executive Summary

becoming available to treat DFUs, more established companies that already offer wound care dressings and medical devices are diversifying their portfolios by adding wound-healing agents through acquisitions and licensing agreements.

High Unmet Need for Efficacious Treatments for Neuroischemic Ulcers

All of the drugs currently in Phase III clinical trials for the treatment of DFUs are being developed to be used in conjunction with standard wound care regimens and are targeted at neuropathic ulcers. KOLs interviewed by GlobalData indicated that the growing subset of chronic, hard-to-treat DFUs that they encounter are neuroischemic and account for more than half the DFU patients they treat. The lack of approved and effective products for the treatment of neuroischemic wounds opens an opportunity for any drug companies that can develop advanced wound therapies for this subset of the DFU population. However, to target the cause of ischemia, further understanding of the role of vascular disease in the development of DFUs will be necessary.

Market Entry of Advanced Wound Care Products Set to Change Treatment Landscape

Over the next five years, the DFU market is expected to see significant changes. With the approval of three wound-healing agents, and the market entry of the first topical antibacterials indicated for diabetic foot infections, physicians will have more options available to them when tackling hard-to-treat ulcers. GlobalData assessed promising pipeline candidates both clinically and commercially, based on the opinions generated from interviews with KOLs and secondary research.

In the wound-healing segment of the market, as illustrated in below mentioned figure Macrocure’s CureXcell and Derma Sciences’ DSC127 have the most favorable clinical attributes, as clinical trial data are already available for both drugs, from post-marketing studies involving CureXcell in Israel, where it is already marketed, and from a Phase II trial of DSC127. Safety reports have also been positive so far, and both drugs have been praised by KOLs for having off-loading standardized in their respective clinical trials. However, in terms of commercial attractiveness, CureXcell’s developer, Macrocure, will struggle due to a lack of experience in the wound care market. Despite this setback, KOLs interviewed by GlobalData still believe that CureXcell is the most unique and promising of the late-stage pipeline agents currently in development. If Macrocure is able to obtain a licensing partner to aid in the
development and marketing of its product, CureXcell would be an ideal therapy for chronic hard-to-heal DFUs.

In the diabetic foot infection segment of the market, the topical antibacterial agents that are currently in development, Innocoll’s Cogenzia and Dipexium Pharmaceuticals’ Locilex, will struggle to compete with systemic broad-spectrum antibiotics, which are used as the standard of care for patients presenting with infected DFUs. Cogenzia is in development as an adjunct to systemic antibiotic therapy, while Locilex is only in development for the treatment of mild diabetic foot infections. Despite the availability of strong clinical trial data on Locilex’s efficacy, KOLs nonetheless believe that Cogenzia is the more interesting of the two pipeline agents due to the product’s novel use of a collagen sponge to deliver an antibiotic locally to a wound site. However, GlobalData believes that if Cogenzia is priced too high, its uptake may be limited, unless the company can demonstrate impressive efficacy compared with the currently available antibiotic therapies.
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What Do Physicians Think?

The KOLs interviewed for this report highlighted that one of the greatest concerns related to the treatment of DFUs is that optimal standard wound care is not provided to all patients. In particular, off-loading, which is considered the “gold standard” in DFU treatment, is grossly underutilized.

“They treat these patients with expensive pharmacologics or even inexpensive pharmacologics, and it’s not just about putting those things on the wound. Those things are not going to help the wound heal faster unless the pressure has been taken off. It’s ironic because these modalities are out there, these off-loading shoes are available, but people aren’t using them as much as they should.”

US Key Opinion Leader, September 2013

KOLs indicated that diabetic patients with neuroischemic wounds are a growing subset of the chronic, hard-to-treat DFUs that they encounter, and that none of the drugs currently in development address this unmet need.

“In the past, we had believed that most patients are mainly neuropathic, and vascular disease played a limited role in terms of healing. What’s changed now is that we are seeing patients that have varying degrees of neuropathy and vascular disease, which together really does greater damage to wound healing than just neuropathy alone.”

US Key Opinion Leader, September 2013

“...The real need in treatment right now is neuroischemic ulcers; neuropathic we can heal with off-loading and a boot.”

EU Key Opinion Leader, September 2013

KOLs interviewed by GlobalData indicated that Regranex, the only marketed pharmacological treatment for DFUs, is not widely used due to its poor efficacy.

“I would estimate very few physicians are using Regranex as a first-, second-, or third-line therapy. It is just not being used in our treatment protocol.”

US Key Opinion Leader, September 2013

“...We currently don’t use it because it’s not present on the market, but we never used it in the past either, both because it was very costly and its effectiveness was not proved.”

EU Key Opinion Leader, September 2013

KOLs discussed the need for well-designed clinical trials for DFU treatments; they emphasized that trials should standardize off-loading and enroll patient populations that are more representative of the actual DFU prevalent population.

“Off-loading is the biggest confounding variable of any trial.”

EU Key Opinion Leader, September 2013
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"Clinical trials need to include the most realistic patient population in product studies, because previously, [the] industry has done a bad job of leaving patients out and only selecting a few patients that they believe are going to benefit most from their product. This is not a true replication of the real-world setting."

US Key Opinion Leader, September 2013

The consensus among KOLs was that of the limited products currently in development, CureXcell was the most promising of the late-stage wound-healing agents.

"The science that is out there and the experience from the Middle East, from Israel, has very promising results. I think it’s unique in its class and there’s nothing like it out there. So, I think it’s promising."

US Key Opinion Leader, September 2013

“If approved, I would absolutely be certain that it would target anybody with non-healing wounds, and in my patient population, that would probably be at least 30% to 50%.”

US Key Opinion Leader, September 2013
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10.6.2 Senior Epidemiologist

10.6.3 Therapy Director – CVMD and Infectious Disease

10.6.4 Global Head of Healthcare

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2 Introduction

2.1 Catalyst

Diabetic foot ulcers (DFUs) are a common complication of diabetes, and with the increasing prevalence of diabetes across all markets, the number of patients suffering from DFUs is also expected to rise. Despite the availability of various treatment modalities, there are currently few advanced wound care products available to treat hard-to-heal chronic wounds. In addition, for the past 15 years, Regranex (becaplermin) has been the only pharmacologic wound-healing agent available; however, it is rarely used due to a perceived lack of efficacy.

The DFU market is now set to enter an exciting phase with the potential launch of three wound-healing agents in the next five years:

- If Olympus Biotech’s trafermin is successful in gaining regulatory approval in the EU, it will be the only growth factor other than Regranex to be approved for the treatment of DFUs, and is expected to launch in 2015.
- Macrocur’s CureXcell, a suspension of activated leukocytes that are injected directly into the wound bed, is expected to launch in the US in 2017. Unique in its class, if approved, it will be the first cellular therapy indicated for DFUs.
- Derma Sciences is developing DSC127, an angiotensin analog reported to accelerate healing by increasing vascularization. It is expected to launch in the US in 2017.

The first two topical antibacterials, Innocoll’s Cogenzia (gentamicin-collagen sponge) and Dipexium Pharmaceuticals’ Locilex (pexiganan acetate cream 1%), are also expected to launch in the US and the five major EU markets (5EU) in 2015 and 2016, respectively. Both pipeline agents offer an alternative way to treat infection by localizing an antibiotic directly at the wound site.

With the advent of these new product launches, the size of the DFU market is expected to grow substantially during the five-year forecast period.
Introduction

2.2 Related Reports

- GlobalData (2013). PharmaPoint: Type 2 Diabetes – Global Drug Forecast and Market Analysis to 2022, July 2013, GDHC55PIDR

2.3 Upcoming Related Reports

Appendix

10.7 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.

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