Below mentioned table presents the key metrics for type 1 diabetes (T1D) in the eight major pharmaceutical markets (8MM) (US, France, Germany, Italy, Spain, UK, Japan, and Canada) during the forecast period from 2013–2023.

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**Type 1 Diabetes Market Will Double by 2023**

GlobalData estimates the 2013 sales for T1D at approximately $6.6 billion across the 8MM covered in this report. The US contributed 74% of these sales, generating an estimated $4.8 billion. This is mainly due to the much higher prices of insulins in the US and a relatively high diagnosed prevalence of T1D in this country compared with the 5EU (France, Germany, Italy, Spain, and UK) and Japan.

The T1D market will approximately double over the forecast period, reaching $13.6 billion at a Compound Annual Growth Rate (CAGR) of 7.6%. This growth will be fueled by the significant increase in T1D prevalence as well as the uptake...
Executive Summary

of the novel ultra-long-acting insulin analogs, novel ultra-rapid formulations of insulin analogs, and the adjunct therapies for T1D. The launches of these novel products will offset the dip in sales caused by the patent expiries of seven insulin products, and the consequent emergence of biosimilars. Human insulins and insulin analogs will remain front-line therapies for T1D as none of the therapies on the horizon will have the capacity to lead to the full regeneration of pancreatic beta cells. Although some of the emerging technologies in regenerative medicine show a big promise for restoring beta-cell function in T1D patients (such as encapsulation technology that protects islet transplants from the host immune system, stem cell therapies, and whole-organ bioengineering), these therapies will likely not become a reality during the forecast period.

The overall usage of insulin pump (continuous subcutaneous insulin infusion [CSII]) therapy in T1D patients will significantly increase, as clearly indicated by all interviewed Key Opinion Leaders (KOLs) and surveyed high-prescribing physicians. This will lead to a decrease in the total market share of basal (long-acting) insulin analogs, while rapid-acting analogs will be slowly overtaking the T1D market. The ultra-rapid formulations of rapid-acting analogs, which are currently in development, will particularly profit from the increase in the usage of pump therapy, as they better match the physiological profile of prandial insulin and therefore, will be preferable for use in pumps. The high possibility of the artificial pancreas becoming a reality during the forecast period will further boost the prospects for ultra-rapid-acting insulin formulations. The long-acting insulin market will decrease from a 38% to 34% share of the total (insulin only) market, while the rapid-acting insulin market will increase from 37% to 42% of the insulin market. Ultra-rapid-acting formulations of insulin analogs, such as Novo Nordisk’s NN-1218 and Adocia’s BioChaperone Lispro, will represent 49% of the whole rapid-acting insulin segment in 2023.

The therapies currently used for type 2 diabetes (T2D) treatment, glucagon-like peptide-1 receptor antagonists (GLP-1 RAs) and sodium-glucose cotransporter 2 (SGLT-2) inhibitors, are expected to be approved for T1D from 2017 and will massively drive the growth of the market, constituting 9% and 11%, respectively, of the total T1D market by 2023. These therapies will not compete with insulins, as they will be prescribed as adjunct, add-on therapies. They will be used particularly in obese T1D patients and patients with a mixed T1D/T2D phenotype. The skyrocketing worldwide obesity epidemic will strongly drive the use of these drug classes for T1D.
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Major drivers for the growth of the T1D market over the forecast period will include:

- Significant increase in T1D diagnosed prevalence, which likely has a major environmental contribution although the reasons behind it are still controversial
- The uptake of novel ultra-long-acting insulin analogs and novel ultra-rapid-acting formulations of currently marketed rapid-acting insulin analogs
- Approval of the currently marketed type 2 diabetes therapies, such as GLP-1 RAs and SGLT-2, for use in T1D patients

Major barriers to the growth of the T1D market will include:

- Biosimilar erosion of the leading insulin brands for T1D treatment, such as Lantus (insulin glargine), Levemir (insulin detemir), Humalog (insulin lispro), and NovoLog (insulin aspart)
- High failure rate of trials for disease-modifying (immunomodulatory or beta-cell preservation) therapies
- Increasing pressure for cost-effectiveness across all markets, which will limit the pricing of new products, and in some cases, prevent their reimbursement

Below mentioned figure depicts the sales for T1D by region throughout the forecast period, 2013–2023.

Major Type 1 Diabetes Players Are Using Various Strategies to Defend Their Blockbuster Franchises from Biosimilar Erosion

Since the discovery of insulin therapy, three major pharmaceuticals companies have been controlling 99% of the global insulin market: Novo Nordisk, Sanofi, and Eli Lilly. Novo Nordisk’s insulin portfolio covers insulin from all existing classes: human insulin, rapid-acting, long-acting, ultra-long-acting, and premix analogs. In addition, the company is
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currently developing an ultra-rapid formulation of its insulin analog NovoLog. Sanofi and Eli Lilly do not have an equally wide-ranging portfolio as Novo Nordisk, but Sanofi’s basal insulin Lantus is the world’s number-one selling insulin brand in terms of both sales and units, while Eli Lilly has the next-generation ultra-long-acting basal insulin in development.

Novo Nordisk, Sanofi, and Eli Lilly are undertaking various strategies to defend their franchises from upcoming biosimilar erosion, as they all faced or are facing patent expiry for their blockbuster insulin analogs (NovoLog, Lantus, and Humalog, respectively). Eli Lilly already has a biosimilar version of Sanofi’s Lantus, which was recently approved in several markets. Sanofi, in turn, is developing a superior version of Lantus, which has been named Toujeo, in order to protect its own franchise from biosimilar erosion. Sanofi is also stepping up its biosimilar insulin development program and expects to have two projects in clinical development soon that are likely to be versions of Eli Lilly’s Humalog and Novo Nordisk’s NovoLog. Only Novo Nordisk is without a biosimilar insulin strategy; however, it does have a recently marketed novel ultra-long-acting insulin analog and an upcoming novel ultra-rapid insulin formulation in development, which will both likely become blockbusters.

The dynamics of the insulin market will not change drastically over the next 10 years in terms of the current and future players in the T1D market and GlobalData expects that Novo Nordisk, Sanofi, and Eli Lilly will continue ruling this space. However, there will be several new entrants in the biosimilar insulin space, such as Merck and Mylan, which will steal a small patient share from the major players. The reason why GlobalData expects a relatively small patient share for biosimilars is that the know-how of the three dominant manufacturers cannot be acquired easily. In addition, they will face competition in improved novel formulations of the same insulins they are trying to produce. Some of the “T2D only” players, such as AstraZeneca, will also likely enter the T1D space over the forecast period with their GLP-1 and SGLT-2 therapies. The crowded GLP-1 RA and SGLT-2 market makes it hard at the moment to define the clear future leaders in this segment, especially in light of the fact that the current T1D leaders have GLP-1 RA and SGLT-2 franchises of their own.

Three biotech companies, Adocia, Biodel, and Halozyme, have some promising ultra-rapid-acting insulin formulations in late-stage development. However, if these formulations are proven successful, it is very likely that these companies will be acquired by major players, such as Novo Nordisk, Eli Lilly, or Sanofi. As Sanofi is a potentially dominant player in the future artificial pancreas market, due to its partnership with Medtronic, the company will need to add an ultra-rapid-acting insulin formulation to its portfolio and it is likely to achieve this by acquiring one of these biotech companies. Most recently (on December
19, 2014), Eli Lilly and Adocia announced a worldwide licensing collaboration focused on developing ultra-rapid insulin, BioChaperone Lispro, for treatment in people with T1D and T2D.

Below mentioned figure provides a company gap analysis in the T1D market during the forecast period.

![Company Portfolio Gap Analysis in Type 1 Diabetes, 2013–2023](Source: GlobalData)

Current Therapies Leave Unmet Needs in Type 1 Diabetes Market

Since its discovery almost 100 years ago, insulin therapy has been the cornerstone of the T1D treatment. The advances in insulin therapies, such as the development of analogs and the novel approaches to the administration of insulin, continuous glucose monitoring (CGM), and improved devices for blood glucose testing have all contributed to the better treatment of T1D patients.

Nevertheless, the majority of T1D patients do not achieve the glycemic targets set by national and international guidelines, and as such, the overall life expectancy in T1D patients is still 10–15 years less than in the healthy population. Therefore, there are considerably high unmet needs within the indication. Overall, these unmet clinical needs are interrelated. One of the largest unmet needs is a need for therapies that would interfere with the pathogenic processes involved in the eradication of the beta cells in T1D patients. Other unmet needs include hypoglycemia avoidance, weight loss and control of the associated metabolic syndrome, treatment for brittle diabetes, and increased patient compliance.

The Market Entry of Ultra-Rapid-Acting Insulin Formulations Will Improve the Treatment Landscape for Type 1 Diabetes Patients

Some therapies and medical devices in development for T1D will partially fulfill some of the unmet needs in this space. Regarding pharmaceuticals in development, the ultra-long-acting insulin analogs and ultra-rapid-acting formulations of insulin analogs are showing the greatest promise in fulfilling the need for hypoglycemia avoidance. According to interviewed KOLs, the latter formulations are a particularly hot topic in the T1D space in the context of their use in a closed loop system (artificial pancreas). Ultra-rapid-acting insulins would better match the physiological profile of prandial insulin by providing a better response to the rapid increase in insulin
need after a meal. GlobalData interviews with KOLs indicated that these formulations are eagerly awaited and that they will bring the artificial pancreas one step closer to reality. Once artificial pancreas use becomes the standard treatment for T1D, ultra-rapid-acting insulins will likely be the major therapeutic option for these patients. Nevertheless, the ultimate need for novel and safe therapies that would prevent pancreatic islet autoimmunity or halt progressive beta-cell destruction will persist and present a big opportunity for drug developers to fulfill the remaining gaps.

Apart from the novel insulin analogs and formulations, the T2D therapies such as GLP-1 RAs and SGLT-2 inhibitors, are expected to further improve the treatment landscape for T1D patients. The epidemic of obesity among T1D patients and an increasingly common occurrence of a mixed T1D/T2D phenotype will strongly drive the use of these therapies.

Below mentioned figure provides a competitive assessment of the late-stage pipeline agents in T1D during the forecast period.

**Big Opportunity Persists for Beta-Cell Regeneration Therapies**

Completed and ongoing intervention trials thus far have not been successful in terms of pancreatic islet autoimmunity prevention and preservation of beta-cell function. These trials have often been designed based on the preclinical findings in animal studies, and it is now clear that the etiology and pathophysiology of T1D is different between rodents and humans. With the advances in understanding the early stages of the etiology and pathogenesis of T1D, there is a hope that future intervention trials will be designed on the basis of
this knowledge. In C-peptide positive patients who still possess some functional pancreatic islet beta cells, adjunct therapies are focused on immunomodulatory approaches to restore beta-cell self-tolerance. Apart from immunomodulatory therapies, there is also interest in the potential application of incretin-based therapies, such as GLP-1 agonists, on C-peptide positive patients, as these therapies may prevent beta-cell apoptosis and enhance beta-cell regeneration. Despite the fact that GLP-1 agonists might fulfill a portion of this large unmet need for the disease-modifying treatment that would prevent islet autoimmunity and halt or reverse progressive beta-cell destruction, this type of treatment will likely remain a challenge. As knowledge about T1D etiology is accumulating rapidly and immune surrogate endpoints to clinical and metabolic outcomes are increasingly defined, it will soon be possible to more comprehensively evaluate trial results. In addition, this knowledge will lead to improved enrollment strategies based on pretreatment immune profiles associated with clinical benefit. There is a big window of opportunity for drug manufacturers to develop disease-modifying therapies, which will almost certainly have to be personalized, both in terms of therapeutic agent and of treatment dose and duration. This personalized approach will have to be based on pretreatment staging and immune monitoring during treatment.

What Do the Physicians Think?

The KOLs interviewed for this report highlighted that there seems to be some environmental factors that influence the rise in T1D prevalence, however, the exact cause of this increase is still unclear.

“I spend every day of my life thinking about it [why the T1D prevalence is increasing]. I have spent 25, 30 years of my life studying the research. That’s what I do. We have no idea what it is, but clearly, it’s either a loss of [immunological] protection, or there is some environmental factor that is leading to this increase. Certainly, in the United States, [the prevalence is increasing] between the ages of 10 and 20; and in the rest of the world, particularly under the age of 10. We don’t really know what this increase is due to.”

US Key Opinion Leader

“This is, of course, a highly controversial question [regarding the increase in T1D prevalence]. Yes, there are some people who are saying that there is earlier diagnosis as a point, in earlier years we didn’t do the autoimmune markers; many of the patients that we thought would be adult type 2 diabetes were actually type 1. But personally, I think no, there must be more to it, and I have the feeling that maybe sometime in the future we will find some environmental agent, maybe some infectious agent that contributes in the whole pitch of autoimmunity. But in general terms, it’s a puzzle of certain genetic susceptibility, unknown
environmental factors, certain viruses, and also some nutrition factors."

OUS Key Opinion Leader

One important point about the current insulin analog market, which was highlighted by many KOLS, is that the choice of the insulin, particularly in the rapid-acting insulin segment, is driven by what is included in the formularies.

“I will use whatever the insurance company has a preference for. If the insurance company says, “Use the NovoLog product,” I’ll use the NovoLog products. If they say, “Use the Lilly product,” I’ll use the Lilly product. If they say, “Use the Sanofi product,” because they’ve negotiated better rates, I’ll use that. I think that the current analog insulins, the faster-acting, are bioequivalent.”

US Key Opinion Leader

KOLs also indicated that CGM has not yet penetrated the clinical routine, but is going to increase tremendously over the coming years, in parallel with the development of the artificial pancreas, where CGM, a control algorithm, and an insulin pump device are combined. These developments will strengthen the need for insulins that are even faster-acting than the currently marketed fast-acting insulin analogs.

“Very few people, to this point anyway, have been – particularly in children – on continuous glucose monitoring systems. They’re certainly on blood glucose monitoring systems, but very few. But it’s increasing. I think continuous glucose monitoring systems is going to increase tremendously over the next few years.”

US Key Opinion Leader

“We have been seeing really an enormous increase in insulin pumps in [European country] from the year 2000 in children. In 2000, there were hardly any pumps and now we have 50% of the kids on [a] pump in our hospital... With pumps becoming more and more convenient, and then with more rapid-acting analogs, which may allow even greater flexibility, I think pump treatment has a bright future, particularly if you look at the closed-loop approaches [artificial pancreas].”

OUS Key Opinion Leader

“Absolutely, no question about it; that is exactly what’s needed – smarter insulins and ultra-fast insulins. There’s no question that that’s what’s going to be needed.... The currently marketed insulins are not very good. They’re okay, they’re better than regular [human insulin], but they really aren’t enough physiological.”

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Another main point that KOLs highlighted is the potential of the use of adjunct therapies, such as GLP-1 RAs and SGLT-2s, in the T1D patient population.

“There’s a big space for using adjunct therapies in type 1, in addition to insulin. Certainly, with as much obesity as we have, there’s a market for those drugs to be used in these patients who have a mixed [T1D/T2D] picture anyway. I know there’s great interest in using GLP-1 agonists or SGLT-2 inhibitors as adjuncts in type 1.”

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“There’s a lot of insulin resistance in type 1 patients as they get more obese and acquire metabolic syndrome type of parameters. So, the short answer is: I think there will be a lot of interest in [both SGLT-2 inhibitors and GLP-1 RAs] and the focus in pharma right now on type 1 intensive therapies is tremendous. So, I think that there is going to be a lot of demand for them and I think that there’s a very high likelihood of them being efficacious, both the incretin class and the SGLT-2 inhibition class.”

US Key Opinion Leader
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Introduction

2 Introduction

2.1 Catalyst

Over the last 90 years, the insulin therapy for type 1 diabetes (T1D) patients has gone through many modifications, as at present, no other treatment can be offered to a patient diagnosed with this disease. A variety of insulin analogs with different times of action – long-acting as well as short or rapid-acting – have been on the market for the past decade. In addition, many other developments were happening in parallel, such as self-monitoring of blood glucose (SMBG) and significant advances in insulin delivery systems. There is a rapidly increasing interest in a closed-loop system, or “artificial pancreas,” where continuous glucose monitoring (CGM), a control algorithm, and an insulin pump device are combined; this, in turn, strengthens the need for insulins that are even faster-acting than the currently marketed rapid-acting insulin analogs, because the ability of closed-loop algorithms to tightly control glucose is limited by the slow speed of available rapid-acting analogs.

Due to the imminent patent expiry of the majority of the currently marketed insulin analogs, biosimilar erosion is on the horizon; however, several companies are developing the highly needed novel ultra-rapid-acting formulations of the marketed insulin analogs to either protect their own franchises from biosimilar erosion, or to capitalize on the upcoming patent expirations of the competitors’ products. On the other side of the spectrum, there are novel ultra-long-acting insulin analogs, recently marketed or in development, which threaten to overtake the basal (long-acting) insulin segment, as the ultra-long-acting insulin analogs show lower hypoglycemic rates and offer higher flexibility in administration.

Along with the significant increase in T1D prevalence worldwide, the uptake of these novel ultra-long-acting insulin analogs and the novel ultra-rapid-acting formulations of the currently marketed rapid-acting insulin analogs will strongly drive the T1D market growth. In addition, the expected approval of the currently marketed type 2 diabetes (T2D) therapies, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter 2 (SGLT-2) inhibitors for use in T1D patients, will further boost the size of the T1D market, which will, due to all these catalysts, double over the next decade.
Introduction

2.2 Related Reports

- GlobalData (2013). Obesity – Global Drug Forecast and Market Analysis to 2022, November 2013, GDHC50PIDR

2.3 Upcoming Related Reports

Appendix

11.7 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, San Francisco, Boston, London, India, Korea, Japan, Singapore, and Australia.

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