

Potential of GLP-1 Agonist in Type-2 Diabetes Mellitus in US

By

Nivreti Pandit

*Dissertation submitted in partial fulfillment of the requirements of the degree
MBA Hospital and Health Management*

Academic year, 2017-2019



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TO WHOMSOEVER MAY CONCERN

This is to certify that **Ms. Nivreti Pandit**, student of MBA Hospital and Health Management from The IIHMR University, Jaipur has undergone internship training at **PharmaACE Analytics, Pune** from **4th Feb 2019 to 3rd May 2019**.

The Candidate has successfully carried out the study assigned to her during internship training and her approach to the study has been sincere, scientific and analytical.

The Internship is in fulfillment of the course requirements.

I wish her all the success in her future endeavors.



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17 May 2019

The certificate is awarded to

Ms. Nivreti Pandit

In recognition of having successfully completed her internship in the department of

Market Research

And has successfully completed her project on

"The potential of GLP-1 inhibitors in Type-2 Diabetes Mellitus in US"

3rd May 2019

She comes across as a committed, sincere and diligent person who has a strong drive and zeal for learning.

We wish her all the best for her future endeavors!



For PharmaACE Innovations LLP

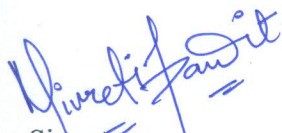
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CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled **"The potential of GLP-1 agonist in Type-2 Diabetes Mellitus In US"** and submitted by **Nivreti Pandit** Enrollment No **IIHMR-U/01/2017-19/0616** under the supervision of **Dr. S.D. Gupta** for award of MBA in Hospital and Health Management of the University carried out during the period from **4th February 2019 to 3rd May 2019** embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other institute or other similar institution of higher learning.


Signature

Acknowledgement

I wish to express my sincere gratitude towards Mr. Dinesh Pandey, Sub-practice Head (Business Analytics) for providing me an opportunity to do my internship at Pharmaace Analytics, Pune.

I would like to thank Ms. Sakshi Garg, Consultant and my coach for continuously guiding me throughout the project and assisting me whenever I needed any help. I also wish to thank all my colleagues and managers who were always ready in providing valuable information vital for the completion of the project.

I sincerely thank Dr. S. D Gupta, Chairman and my guide for supporting me throughout my study course and suggesting topics which can become a potential study area.

I would like to thank Dr.Sandesh Sharma, Associate Professor and my mentor, for encouraging and guiding me about the organization and assisting me in choosing the necessary study topics.

Lastly, I would like to thank my parents, and my co-trainees for making this training course joyful but always efficient

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Abbreviations

- **GLP-1:** Glucagon Like Peptide-1 receptor
- **DPP-4:** Dipeptidyl Peptidase 4
- **SGLT-2:** Sodium-glucose Transport Protein 2
- **AACE:** American Association of Clinical Endocrinologists
- **ACE:** American College of Endocrinology
- **DM:** Diabetes Mellitus
- **SU:** Sulphonylureas
- **IGT:** Impaired Glucose Tolerance

The Potential of GLP-1 Receptor Agonist in Type-2 Diabetes Mellitus In US

Abstract

Title: The Potential Of GLP-1 Receptor Agonists in Type-2 Diabetes Mellitus In US

Author: Nivreti Pandit

Background of the Study

The aim of the study is to assess the potential of GLP-1 Agonists in Type-2 Diabetes Mellitus In US. The study was based on secondary research from different data sources. There are various GLP-1 Agonists approved for the treatment of diabetes in US. These include lixisenatide (once daily), exenatide and liraglutide. The other GLP-1 Agonists include extended-release exenatide (once weekly), dulaglutide and albiglutide. These drugs have shown a decrease in the HbA1c levels by ~0.8-1.6%. The GLP-1 Agonists decrease weight in diabetic patients by ~1-3 kg. These drugs have an increased advantage of lowering lipid and blood pressure levels. These drugs have demonstrated greater efficacy in the treatment of patients suffering from type 2 Diabetes Mellitus. GLP-1 Agonists have an added benefit as they can be given alone or in combination with other anti-hypertensive drugs.

Objectives

- To study the competitive landscape of GLP-1 in diabetes market
- To determine the key products and players in the diabetes market
- To estimate the market value and market volume of GLP-1 in Type-2 Diabetes Mellitus

Methodology

The descriptive and exploratory study was conducted at Pharmaace Analytics, Pune which involved assessment of the total diabetes market in US. A rigorous secondary research was done with inference concluded from different databanks, research papers, books, journals and websites to collect the data. The prevalence of diabetes patients across the globe including US was determined. The assessment of healthcare burden associated with diabetes was determined. The study also included analysis of pricing practice for diabetes blockbuster drugs which would give an idea about the diabetes drug market space. The study involved analysis of the treatment landscape to assess the key products and players currently leading the diabetes market. Diabetes product sales forecast was analyzed from different data sources to estimate the future sales of GLP-1 drugs in diabetes. Pipeline analysis indicating the potential drugs in the GLP-1 drug class was estimated. Sales data analysis of different drug class used in diabetes treatment was analyzed to estimate the diabetes market volume. Based on the above analysis, the study was concluded with the discussion about potential scope of GLP-1 in the diabetes market.

Results- In the GLP-1 market space, Victoza (GLP-1) leads the diabetes market currently, and Novo Nordisk came up with a once-weekly formulation called Ozempic. According to the company website, in the category of new-to-brand prescriptions, Ozempic represents 26% of the market share. In addition to this, another oral GLP-1 (expected to launch in 2020) would boost up the sales of GLP-1 Agonists in the diabetes market.

Conclusion- GLP-1 Agonists can be an effective treatment options for type 2 diabetes mellitus patients as they achieve greater reductions in the A1C levels. They cause a potential decrease in the body weight and can be used in patients who are non-responsive to oral anti-hyperglycemia drugs.

Keywords- GLP-1 (Glucagon-Like Peptide-1), DM (Diabetes Mellitus), A1C (Haemoglobin A1c)

Introduction

Diabetes mellitus is a disease of the endocrine system characterized by an acquired or inherent deficiency of insulin production by the pancreatic cells. Diabetes also occurs as a result of the ineffectiveness of the produced insulin to decrease glucose levels in the body. Due to ineffectiveness of acquired insulin to work properly, the blood glucose levels in the body are increased. This increased concentration of blood glucose is responsible for causing potential damage to the body involving various body systems.¹

The different forms of diabetes mellitus include-

- **Type-1 Diabetes Mellitus-** (Also known as insulin dependent diabetes mellitus)- It is a type of diabetes which generally occurs in younger age. It occurs when there is complete absence of insulin due to failure of the pancreatic cells to produce the required amount of insulin required for proper functioning of the body. Type-1 diabetes is most frequently seen in children and young adults but can also be seen in later stages of life.
- **Type-2 Diabetes Mellitus-** (Also known as non-insulin dependent diabetes mellitus)- It results from the inability of the produced insulin to work effectively in decreasing the blood glucose levels. The body does not respond properly to the insulin levels produced by the pancreatic cells. This inability of the insulin to work effectively results in various signs and symptoms. Type 2 diabetes mellitus is relatively more common than Type-1 and it is estimated that approximately 90% of the diabetes patients suffer from type-2 diabetes mellitus. It is seen more commonly in older age group but can be seen in adolescents as well.

Type-1 diabetes can occur due to various gene markers which act as a risk factor for the disease. In different populations, certain genes have been associated with the development of Type-2 diabetes mellitus, and the disease is hereditary in nature.

Diabetes Mellitus is a complex disease characterized by mutations in certain genes and environmental factors.

In addition to this, gestational diabetes can give rise to certain adverse outcomes including birth defect in babies, increased risk of birth weight and an increased risk of maternal mortality. Dietary modifications may be done to reduce the risk of diabetes in gravid mothers.

Impaired glucose tolerance is a state when the patient is at the risk of developing diabetes and has an increased risk of developing cardiovascular diseases. The patients may be in the state of IGT before they develop type-2 diabetes mellitus.

The symptoms of diabetes are marked and can range from frequent thirst to blurred vision.

- The symptoms of Type-1 diabetes include- excessive thirst (polydipsia) and urination (polyuria), unexplained weight loss associated with irritable behavior and fatigue.
- These symptoms of Type-2 diabetes mellitus can range from no symptoms to symptoms including- excessive thirst and urination, increased appetite, tiredness, irritability and blurred vision. The disease is detected at later stages when the undesired complications have already set in.

The main goal of diabetes mellitus treatment involves glycemic control. The backbone of diabetes management is dietary modification and physical exercises. Almost 40% of the patients use oral agents for treatment of diabetes and approximately 40% of the patients use insulin injections to control blood sugar levels. Diabetes is a common chronic disorder which poses a significant burden on the economy of the country. However, if effectively managed, the disease can be effectively controlled and managed and its progression can be halted. Increased awareness regarding the disease and the risk factors would help in preventing and controlling the progression of the disease.

Background and Rationale

GLP-1 is an incretin hormone released from the pancreatic cells and causes insulin secretion from pancreas. It also causes decrease in the glucagon level in the body. Shorter-acting GLP-1 agonist who have a shorter acting mechanism decrease post-prandial blood glucose. The GLP-1 agonist with a longer acting mechanism longer-acting GLP-1 agonists have a greater effect on decreasing post-prandial and fasting blood glucose levels.

Type-2 diabetes patients are more commonly prescribed GLP-1 agonists, particularly those patients who are non-responsive to oral-anti-hyperglycemic drugs. Those patients who show an insufficient response to metformin can also be prescribed GLP-1 agonists. GLP-1 receptors can be taken alone or in combination with other diabetes drugs. The GLP-1 agonists demonstrate higher efficacy than DPP-4 inhibitors according to various studies.

There are various benefits of GLP-1 in the treatment of type 2 Diabetes Mellitus. GLP-1 agonists which are exogenous in nature (intravenous) are more effective in decreasing the blood glucose levels. According to a study, GLP-1 Agonists demonstrate greater efficacy in patients who are non-responsive or show inadequate response to oral antihyperglycemic drugs. The various effects of GLP-1 administration in type-2 diabetes patients include-

- Decrease in the glucagon levels in body
- Reduction in the HbA1c levels
- Improvement in the insulin concentration
- Increased satiety
- Reductions in free fatty acid levels
- Decrease in body weight
- Decreased and slow gastric emptying

GLP-1 usage is associated with various pros and cons. The advantage of using GLP-1 agonists include its relatively lower risk of associated hypoglycemia. GLP-1 agonists have a strong efficacy and cause greater reductions in the HbA1c levels. In addition to its anti-hyperglycemic effect, GLP-1 Agonists have shown

strong weight reduction results. Other possible benefits of GLP-1 Agonists include beta cell preservation and potential cardiovascular benefit.

The property of GLP-1 agonists which can induce non-compliance in patients is its intravenous route of administration. GLP-1 agonists are potentially more expensive than sulphonylureas and metformin drug. GLP-1 agonists can induce nausea and gastro-intestinal side effects with a slight possible risk of pancreatitis.

Byetta, which has been approved for the treatment of diabetes mellitus in May, 2005, has certain advantages over other available therapy - it causes an HbA1c drop of between 0.8 percent and 1 percent (and a drop of 1.5 percent in a recent study), causes weight loss, is not associated with hypoglycemia, and is fairly well tolerated.

Exenatide once-weekly is an approved drug in US which is manufactured using a special technology, so that it can be taken once a week. Exenatide is packed in microscopic balls. These microscopic balls gradually break down releasing the drug. It has shown more efficacy than Byetta.

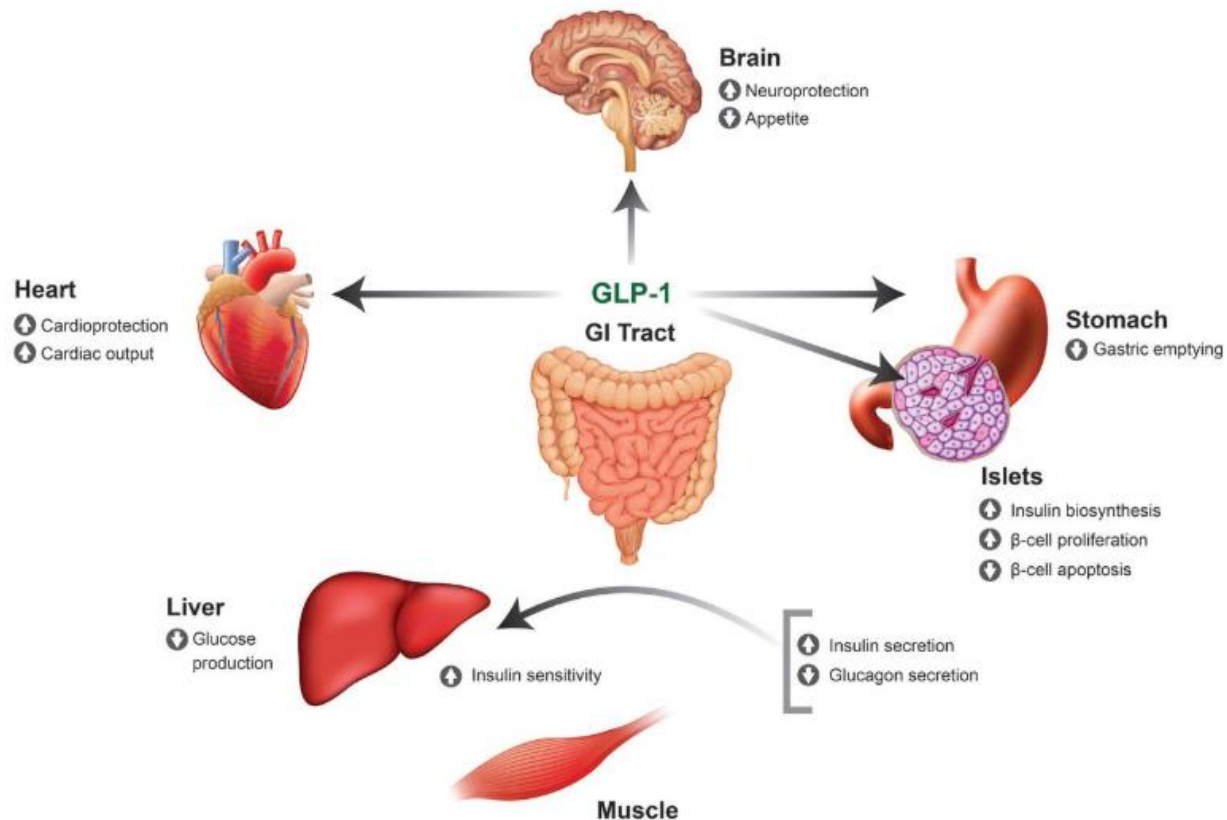


Figure 1: Role of GLP-1 agonists on different organs in the body²

A major reason that this drug class has generated so much interest is the fact that GLP-1 agonists are associated with weight loss. This is the major difference as compared to other drugs for the treatment of type-2 diabetes mellitus, which have shown lesser effects on weight loss.

According to a study, the drug showed a mean weight loss of 1.6 to 2.8 kg. Weight loss is difficult to achieve in patients with type 2 diabetes. According to various studies, obese diabetic patients, using GLP-1 agonists has a mean weight loss of 6kg at 6 months.

GLP-1 agonist drugs have a lower tendency to cause major hypoglycaemia when used in combination with metformin or other anti-hyperglycemic drugs.

There is a shift observed in the choice of drugs prescribed from oral anti-hyperglycemics to GLP-1 inhibitors especially due to their favorable effect on weight loss and cardio protection. Older drugs are being replaced by new and more efficacious drugs with less side effects. Therefore, this study focuses on estimating the potential of GLP-1 in the diabetes market.

- Diabetes is a global emergency with nearly 425Mn people suffering with the disease. Thus, it can be a potential market for gaining maximum benefits.
- The diabetes market is very competitive and fragmented and therefore there is a need to estimate it.
- Decision making in companies are becoming more data driven and therefore market analysis reports are very essential.
- New entrants can evaluate their entry options into such competitive markets for maximum benefits.
- Market insights can help existing players to assess their competitors

Literature Review

Predictors of Effectiveness of Glucagon-Like Peptide-1 Receptor Agonist Therapy in Patients with Type 2 Diabetes and Obesity (Dec 2018)

It is well known that diabetes mellitus (DM) exacerbates the mechanisms underlying atherosclerosis. Currently, glucagon-like peptide-1 receptor agonist (a GLP-1) have one of the most prominent cardioprotective effects among the antidiabetic agents.

This study was done to identify the predictors of the greater impact of aGLP-1 on HbA1c levels, weight reduction, and improvement in lipid profile. The study group consisted of 40 patients with type 2 DM (T2DM) and obesity who were treated with GLP-1. The follow-up period was 24 weeks.

It was concluded in the study that the patients who had initially higher BMI (body mass index), glycemia, and triglycerides (TG) had better improvement in these parameters with GLP-1 treatment. In patients with a BMI loss $\geq 5\%$, GLP-1 and fasting ghrelin levels were higher and ghrelin level in post nutritional status was lower.

The HbA1c levels decreased more intensively in participants with higher GLP-1 levels. It was concluded in the end that the evaluation of the glycemic control, lipid profile levels are useable for estimating the expected efficacy of GLP-1 Agonist.

GLP-1 Receptor Agonists: An Alternative for Rapid-Acting Insulin- A US Pharmacist Report (Oct 2016)

The study focuses on GLP-1 Agonists in the treatment of diabetes mellitus. There have been significant advances in type 2 diabetes mellitus management within the past decade. One of the more recent

developments is the introduction of glucagon-like peptide-1 receptor agonist (GLP-1). The first agent in this class, exenatide, was approved by the FDA in 2005.

This study suggests the pharmacists' approach in determining GLP-1 as an effective treatment option in diabetes.

It concludes that the Pharmacists should use a patient-centered approach and evaluate whether each individual patient would benefit from the addition of a GLP-1 RA as an alternative to thrice-daily prandial insulin injections. To determine if this is the most appropriate treatment, pharmacists should consider the following-

Administration burden: Include frequency of use and timing with meals. GLP-1 RAs are considered to have a lower administration burden.

Efficacy: GLP-1 RAs have been shown to be at least equivalent to prandial insulin in short duration trials with baseline A1C <9%. Patients requiring stronger therapy would likely benefit from intensive insulin titration.

Hypoglycemia: The risk is less with GLP-1.

Weight: Weight loss is seen with GLP-1 RAs as opposed to weight gain with insulin therapy.

Gastrointestinal effects: These are a significant concern with GLP-1 RAs compared to insulin, but tolerance can develop with time

Methodology

It was a descriptive and exploratory research. A rigorous secondary research was done with inference concluded from different databanks, research papers, books, journals and websites to collect the data. Diabetes global sales data was assessed and the data for US was extracted and analyzed to arrive at conclusions.

Research Question

- What is the market potential of GLP-1 in Type-2 Diabetes Mellitus In US?

Objectives

- To study the competitive landscape of GLP-1 in diabetes market
- To determine the key products and players in the diabetes market
- To estimate the market value and market volume of GLP-1 in Type-2 Diabetes Mellitus

Materials and Methods

- **Study Design:** Descriptive and exploratory study.
- **Data Collection Technique:** Review of relevant documents will be done, and qualitative information will be collected based on the resource inputs provided.
- **Data Source:** Secondary sources including Clarivate and Evaluate pharma reports

Duration of the Study

The study was done for a period of three months i.e. from 4th February 2019 to 4th May 2019

Ethical Consideration

- The research will be completed with appropriate research guidelines.
- The confidentiality of the data will be maintained and no information about the companies will be revealed which will potentially disclose their marketing strategy.

Implications of the Research

The study would give us insight of how the market is moving and this would facilitate the companies in deciding the right product which would be more profitable. The company can choose to come up with a highly prescribed molecule with highly prescribed strength and compete in the market using various strategies. The company can also choose to enter into a monopolistic market and try to grab the market share of the existing player. Combination therapy is used in most of the patients therefore combination drugs can also be a feasible market.

Diabetes Mellitus Epidemiology in US

Diabetes is a global emergency with approx. 425 million people (8.8% of adults 20-79 years) living with the disease worldwide. There are 327Mn people of working age group (20-64 years) with diabetes, and 122.8 million people (65-99 years) with diabetes. In 2017, there were approximately 279Mn people in the urban areas living with diabetes and approximately 146 million diabetic patients in the rural area and the prevalence is higher in urban (10.2%) than in rural areas (6.9%).

Diabetes is responsible for 10.7% of mortality in people in all the age groups.

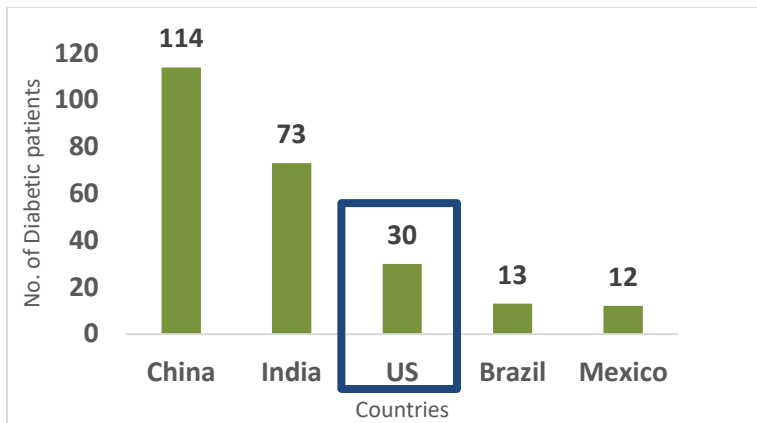
Approximately, 4 million people died from diabetes in 2017.

In the North America and Caribbean region, Impaired Glucose tolerance was seen in approx. 55 million people aged between 20-79 years.

The North American region had a prevalence of approximately 13%. (aged 20-79 years) in 2017.

Out of 46 million people (20- 79 years adults) suffering from diabetes, 17.3Mn diabetic patients are undiagnosed.

Approximately, 176,700 diabetic patients died in 2017 in US, which was the maximum number of diabetes related death in any country across the globe.



Graph 1: Top 5 Countries with Type-2 Diabetic Adult (20-79 years) in 2017

Approximately 30 million Americans aged 20-79 years suffer from diabetes making US among the top 5 countries for the number of people suffering with type-2 diabetes.

China tops the diabetes prevalence with approximately 114 million adults suffering with the disease compared to Mexico which is at the fifth place with an estimated prevalence of 12 million.

Diabetes Market Space- Impact on healthcare systems and revenue spent on Type-2 Diabetes Mellitus

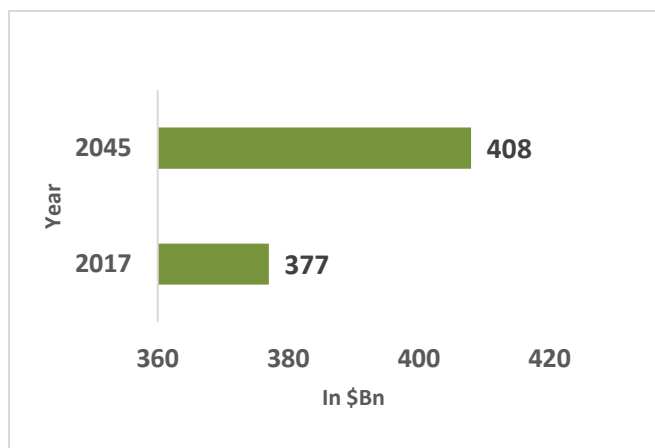
Diabetes imposes a significant economic impact on healthcare systems with nearly ~\$348bn spent in the US alone. The total healthcare expenditure in diabetes was approximately ~\$727Bn in 2017 for people aged between 20 years to 79 years. Compared to the healthcare expenditure in the year 2015, there was an 8% increase in the year 2017.

The total healthcare cost for diabetes was approximately \$850 billion for the diabetic patients aged between 18 years to 99 years.

It is estimated that the healthcare expenditure for diabetes may reach up to \$776Bn in the year 2045.

In the US, the estimated healthcare expenditure due to diabetes mellitus was approximately ID 348 billion trailed by China with ID110 Bn and Germany with ID 42 billion respectively.

US with \$11,683 had the highest healthcare expenditure in terms of per person cost (yearly) in 2017.



Graph 2: Health expenditure by diabetic patients in US (20-79 years)

Diabetes drug pricing practice for medicines with global sales of more than \$1 billion a year

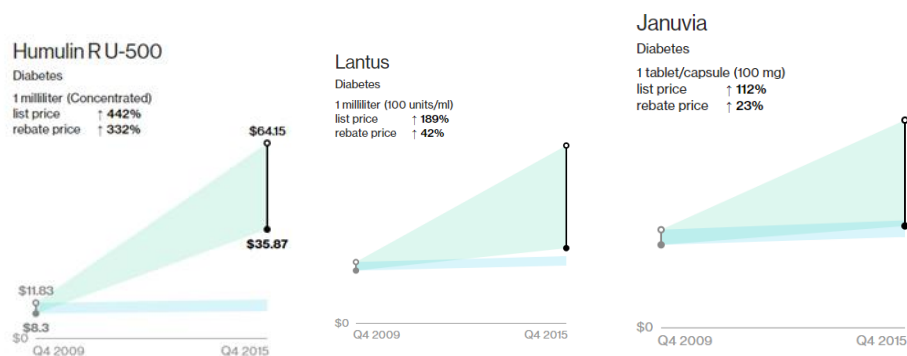


Figure 2: Diabetes Blockbuster drugs Pricing Practice- Humulin, Lantus and Januvia

Discounts vary dramatically, depending on disease type and how much competition exists. Humalog, (a short-acting insulin made by Eli Lilly & Co.) list price increases were wiped out by ever-bigger discounts.

Lilly offered discounts of 66 percent on Humalog last year, up from 23 percent in 2009, according to SSR Health estimates. Lilly provides on an average 35 percent discount for commercial insurance plans and 80 percent for government plans. Novo Nordisk offered over 50 percent discount in for all its medicines, compared with about 35 percent in 2010.

Januvia's after discount price rose by 23% when the inflation was about 9.3% suggesting a price increase slightly above the inflation price. Humulin R U-500 after discount price rose by 332% compared to an inflation of 9.5 percent suggesting pricing practice well above inflation. Lantus price after discount rose by 42% in Q42015 compared to a price of \$8.6 in Q42009 suggesting pricing practice well above inflation.

Humalog had a price increase from \$12.34 in Q4 2009 to \$29.36 in Q4 2015. After discounts, the average price that insurers pay for Humalog increased slightly less than the 9.5 percent rise in inflation over this period. Insurers can easily require patients to switch to alternatives, giving them leverage to negotiate lower prices.

Humalog faces competition from a very similar drug: Novolog, from Novo Nordisk A/S. Discounts for Novolog have risen in a parallel fashion since 2012.

Pipeline Assessment GLP-1

The various GLP-1 receptor agonist in pipeline were explored to determine the competitive threat to this drug class in the diabetes market. Competitive analysis is important to assess the potential of the GLP-1 in the diabetes market space.

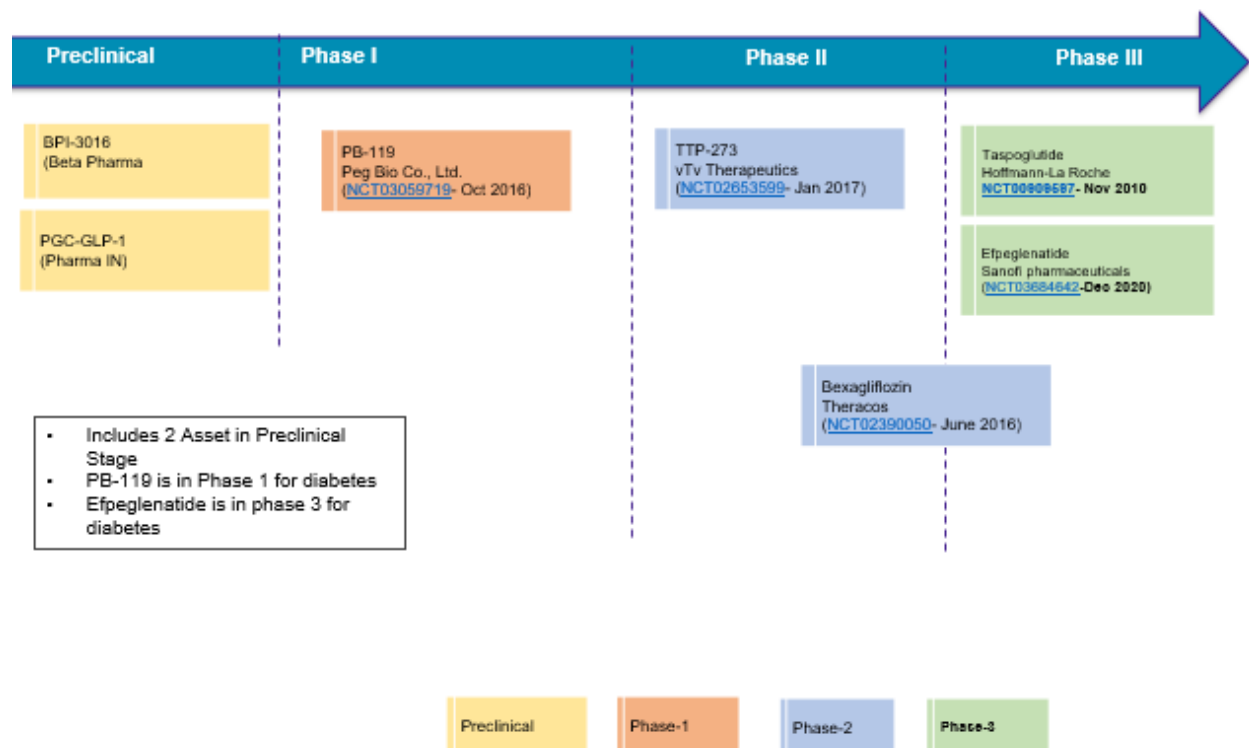


Figure 4- The above picture explains about the various GLP-1 drugs in clinical stage development for Type-2 Diabetes Mellitus

There are more than 5 assets in pipeline for Type-2 diabetes Mellitus. There are about 2 GLP-1 in phase 3 clinical development. This concludes that there won't be much therapies in the future which would provide competition to the GLP-1 drug class in the diabetes market space.

Diabetes Mellitus Treatment Algorithm

Glycemic Management of Type 2 Diabetes Involves Lowering of A1C Levels and Preventing Hypoglycemia

Monotherapy may be effective when the baseline A1C levels are between 6.5%-7.5% (Metformin is the first choice for monotherapy if no contraindications). Dual therapy with metformin provides superior glycemic control over metformin alone (Baseline A1C 7.6% - 9.0%).

If patient is asymptomatic with recent onset of disease and drug naïve, may consider starting with dual or triple oral regimens (Baseline A1C > 9.0%), If symptomatic, start insulin.

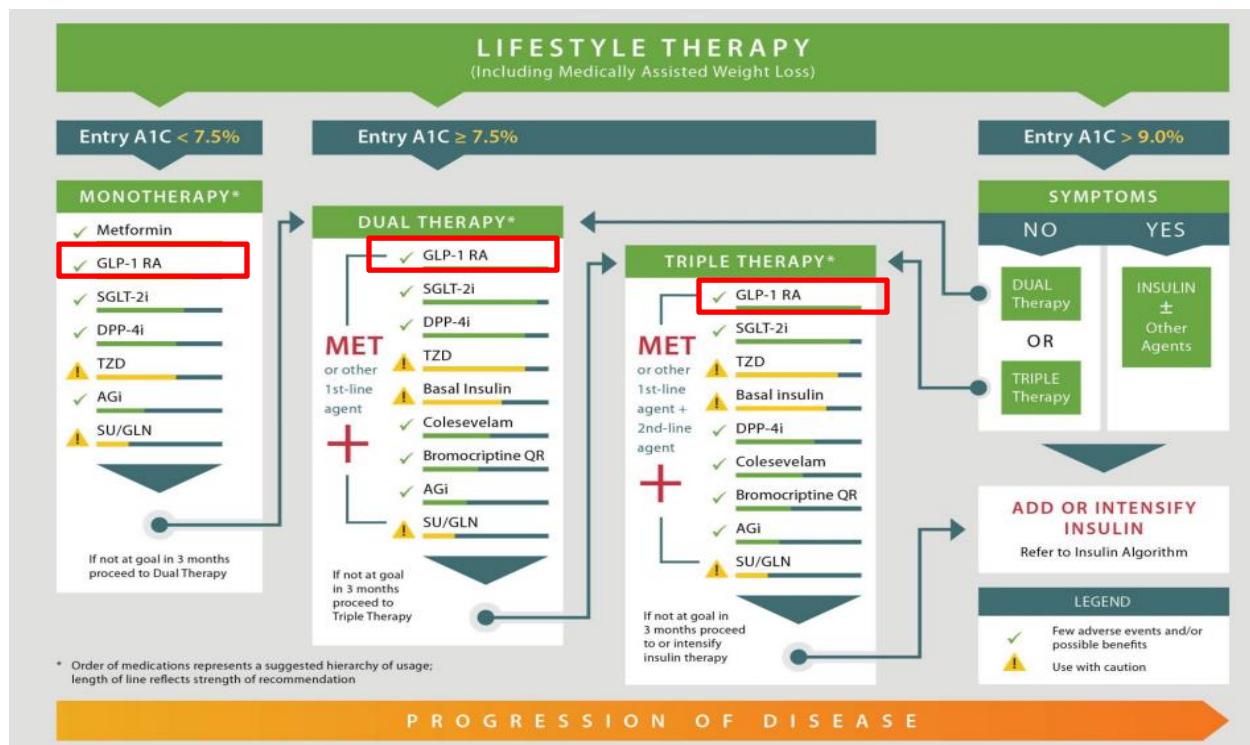


Figure 4- Diabetic Treatment Algorithm according to American Academy of Endocrinology (ACE) and American Association of Clinical Endocrinologists (AACE)

Algorithm to achieve glycemic goals baseline A1c 6.5% - 7.5%- Monotherapy may be effective in this range

- Metformin is the first choice for monotherapy if no contraindications – Consider DPP-4 if PP and FPG, GLP-1 if PP, TZD if metabolic syndrome or NAFLD, AGI if PP – Do not recommend secretagogue (SU or glinide) in this range due to risk of hypoglycemia; short-lived effect
- If monotherapy is unsuccessful, move on to dual oral rx; often need to augment reduction in PP BG to get to goal in this A1C range.

Algorithm to Achieve Glycemic Goals Baseline A1C 7.6% - 9.0%- Dual therapy with metformin provides superior glycemic control over metformin alone. If dual oral rx is unsuccessful, consider triple therapy. If triple oral rx fails to achieve A1C goal, initiate insulin.

Algorithm to Achieve Glycemic Goals Baseline A1C > 9.0%- If patient is asymptomatic with recent onset of disease and drug naïve, may consider starting with dual or triple oral regimens. If symptomatic, start insulin. Once A1C has improved to <7.5%, consider initiation of dual oral therapy with tapering and possible discontinuation of insulin rx.

Diabetes Key Products and Players in The Market

The treatment landscape itself is crowded, with multiple classes and multiple agents within each class with no novel treatments in pipeline. Various GLP-1 receptor agonists are approved in the United States for the treatment of Type-2 diabetes mellitus. Exenatide was approved in the US in 2005 for diabetic patients. An intermediate acting Liraglutide was approved in the US. It is supposed to be administered once daily. Albiglutide and dulaglutide are long acting GLP-1 agonist approved for the treatment of diabetes in US.

The peak concentration of exenatide after administration takes approximately 2.1 hours.

Exenatide is administered within an hour after taking meals.

Lixisenatide is given before the 1st meal of the day. It is given once daily, 1 hour before taking meals. Plasma half-life of the drug is approximately 3 hours.

Liraglutide has a plasma half-life of 12.6 hours. It can be administered anytime without considering meals.

The long acting GLP-1 agonist Albiglutide has a half-life of 5 days.

Dulaglutide also has a half-life of 5 days.

Table1- Summary of US approved GLP-1 Receptor Agonists

Generic Name; Manufacturer	Dosage	Need to be given after meals
Short-Acting GLP-1		
Exenatide; AstraZeneca	Two times a day	Yes
Lixisenatide; Sanofi	Once a day daily	Yes

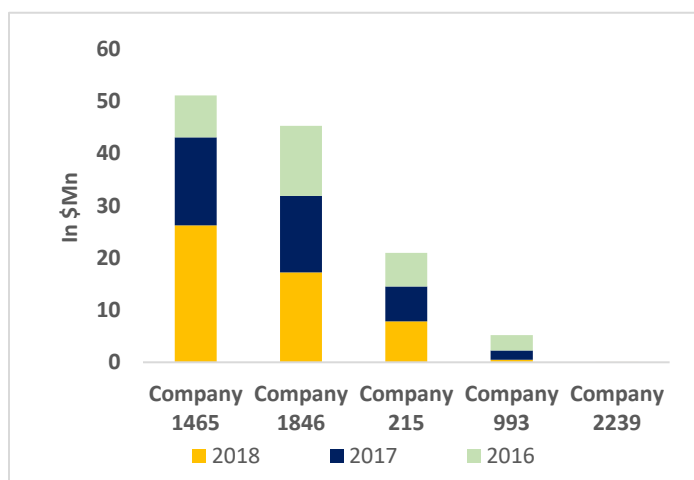
Table2- Summary of US approved GLP-1 Receptor Agonists

Generic Name; Manufacturer	Dosage	Need to be given after meals
Intermediate-acting GLP-1 agonist		
Liraglutide; Novo Nordisk	Once a day	No
Long- acting GLP-1agonist		
Exenatide; AstraZeneca	One time a week	No
Albiglutide; GSK	One time a week	No
Dulaglutide; Eli Lilly	One time a week	No

Diabetes Sales Data Analysis

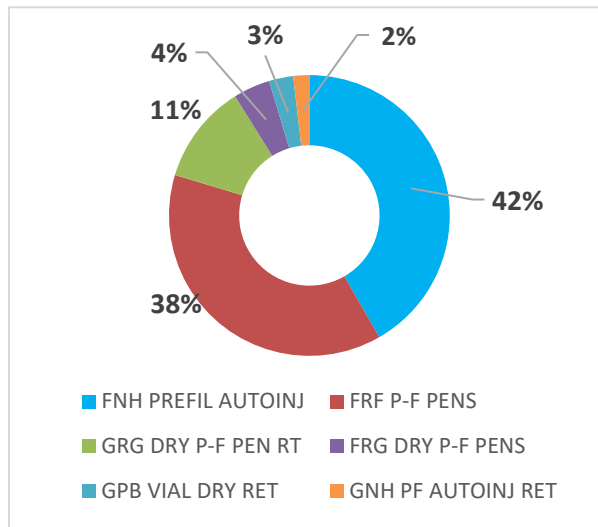
The diabetes global sales data was provided and the sales for US were extracted and analyzed to arrive at conclusion. The sales data included list of companies which were analyzed for different drug class. The drug class analyzed included GLP-1 receptor agonist, DPP-4 receptor agonist and SGLT-2 receptor agonist.

The analysis for GLP-1 receptor agonist was as follows-



Graph 3- Top 5 Companies for Sales in US (Standard Units)

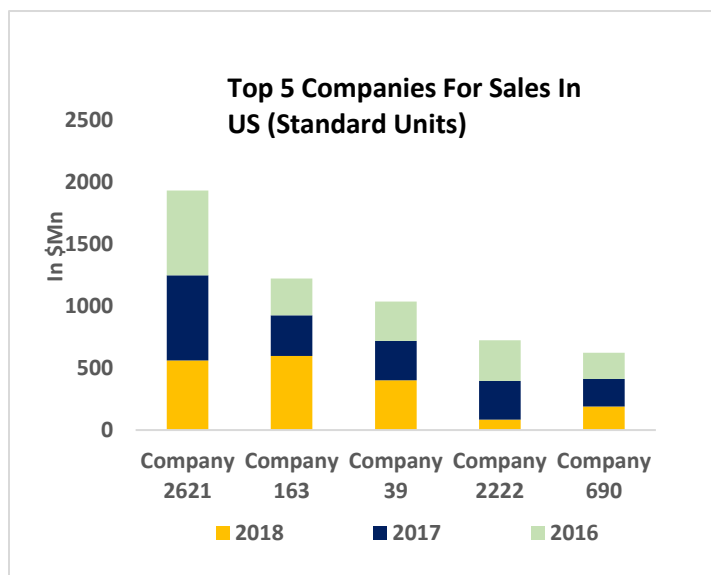
The top five companies in GLP-1 market include- Company1465, Company 1846, Company 215, Company 993, Company 2239. Company 1465 showed the highest sales of ~\$22Mn in 2018. Company 1846 has the highest sales of ~\$4Bn (in terms of manufacturing units) for the year 2016-2018. Company 993 had a negative growth of -52% and - for the year 2016-17.



Graph 4 - GLP-1 Drug Form Sales in US (%)

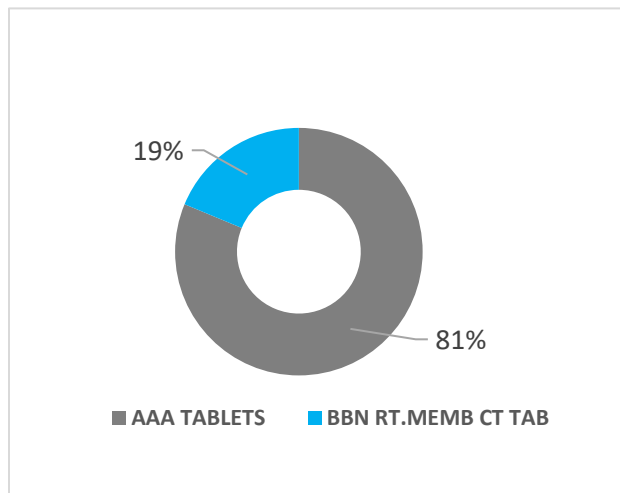
GLP-1 Agonists are dispensed in 6 forms i.e. Pre-filled Auto-injection, FRF Pens, GRG Dry P-F Pens, FRG Dry Pens, GPB Vial and GNH PF Auto-injection. The FNH Pre-filled Auto-injector had the highest sales of 42% followed by FRF P-F Pens for the year 2016-18. Sales of FNH Pre-filled Auto-injector was highest for all the year with sales of ~\$26Mn in 2018. FRF P-F Pens had sales of ~\$17 Mn in 2018.

The analysis for sulphonylurea include-



Graph 5- Top 5 Companies for Sales in US (Standard Units)

The top five companies in Sulphonylurea market includes - Company 2621, Company 163, Company 39, Company 2222 and Company 690. Company 2621 showed the highest sales of ~\$561Mn in 2018. Company 2621 has the highest sales of ~\$4Bn (in terms of manufacturing units) for the year 2016-2018. Company 2222 had a negative YOY growth of -5% and for the year 2016-17.



Graph 6-Sulphonylurea drug form sales in US (%) (2016-18)

The pie chart depicts the analysis of sulphonylureas and explains the percentage share occupied by different drug forms.

Sulphonylureas are dispensed in 2 oral forms i.e. AAA Tablets and BBN RT Memb. CT Tabs.

The AAA Tablets had the highest sales of 81% followed by 19% sales for the BBN RT Memb. CT Tablets for the year 2016-18.

Sales of AAA Tablets was highest for all the year with sales of ~\$1Bn in 2018. BBN RT memb. CT Tabs had sales of ~\$442Mn in 2018.

Suggestion

The branded GLP-1 is facing stiff competition from the other drugs and generics in the market. Hence future market strategy should come up to address this problem.

Conclusion

GLP-1 Agonists have shown superior and statistically significant reduction in diabetes market relative to standard of care with sales forecasted to reach \$3.5Bn by 2022 [2018 sales were ~\$276Mn].

Ozempic (a GLP-1 analog) gained 25% market share when it was launched in US in 2018. (Ozempic is direct to consumer product, which carved out a 5.6% share for the GLP-1 non-insulin antidiabetics market and secured nearly 5,000 new prescriptions by mid-July (within 4 months of launch).

At the end of January 2019, GLP-1 analogue held a 24% share of weekly new-to-brand prescriptions in the diabetes market at the time of its launch, according to IQVIA sales estimates cited by Credit Suisse.

The main GLP-1 Agonists grabbing the diabetes market include- Trulicity (Lilly) and Ozempic (Novo Nordisk). Once-weekly launch of GLP-1 Agonist- Ozempic in 2018 has put Novo on an equal footing with Lilly in terms of convenience and hopes to gain more ground with sales expected to reach \$4.7Bn by 2024.

Another oral GLP-1 is expected to launch in 2020 with greater efficacy results in the clinical trials which is expected to boost up the sales of GLP-1 Agonists in the diabetes market space.

Thus, GLP-1 Agonists with its potential anti-hyperglycaemic effect and weight loss reductions in diabetes mellitus patients holds a greater scope in the treatment of Type-2 diabetes mellitus patients.

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