**SGLT2 inhibitors to take centre stage in 2017?**

**Introduction**

There are few primary care categories as dynamic as diabetes (Type 1 and 2); not only is the category forecast to grow at 6.8% globally through to 2022 as more patients are diagnosed but it is likely to become the second largest category after oncology. More intriguing is that the players in this therapeutic area are relatively few in number and yet their competitive position in key geographies belies their marketing strength in other markets or treatment categories. This is particularly true in the UK oral anti-diabetes market. While early market entry and strong clinical data would be the expected drivers of market share there are many examples in the dynamic Type 2 sub-categories of DPP4 and SGLT2 inhibitors where UK market shares differ markedly from those in the US, raising serious questions about marketing strategies and capabilities. The rest of this paper will explore some of these issues and provide some suggestions as to how companies may alter course if they are to maximise the commercial opportunities available to them.

**FIGURE 1: RELATIVELY FEW PLAYERS IN DIABETES MARKETS**

There are seven key players within the global Type 2 oral market that sell DPP4 and SGLT2 inhibitors. (see Figure 1). For clarity NovoNordisk, Sanofi and Bayer have been removed from Figure 1 since they are mainly involved in other categories of Type 2 drug. Figure 1 shows that private company Boehringer Ingelheim is forecast to grow the fastest and have a Type 2 diabetes franchise in 2022 second only to Merck & Co in scale, surpassing AstraZeneca, Janssen (J&J’s Pharma Division), Novartis, Takeda and even Lilly when the latter’s insulin sales are stripped out. These seven players will be the subject of the rest of this paper, in particular with respect to their positions within the DPP4 and SGLT2 inhibitor market.

**Competitors’ performance in the UK belie their traditional strength**

The SGLT2 inhibitors for Type 2 diabetes create additional options for patients, doctors and pharmaceutical companies. As a sub-category that began commercial life in 2011 it took off in 2015 when three competitor products achieved aggregate sales of $2bn. The sales forecast for this sub-category in 2022 is around $9bn. With clinical data, backed up by a label claim, suggesting that empagliflozin (Jardiance) reduces cardiovascular risk, with similar data for dapagliflozin (Forxiga) and canagliflozin (Invokana) still to come,

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1 Evaluate Pharma – World Preview 2016, Outlook to 2022
these sales forecasts may not be unrealistic. However, forecasting the allocation of future sales between each of the competitors, Janssen (Johnson & Johnson), Astra Zeneca and Lilly/Boehringer Ingelheim (the last two are co-promoters of empagliflozin and linagliptin) may not be as straightforward as the forecasts suggest.

One complication is the competitive strength of the earlier class of Type 2 anti-diabetics, the DPP-4 inhibitors, dominated by Merck’s sitagliptin (Januvia) franchise. Furthermore, the Type 2 area is dogged by access and discounting concerns in the US. While AZN’s dapagliflozin sales are fairly evenly split between US and ex-US, Janssen’s canagliflozin is massively skewed to the US. AZN claims global SGLT2 volume leadership with a 42% share but can muster just 26% of total value\(^2\). Within the DPP-4 class AZN, Merck and the Lilly/BI partnership all have decent sales globally but AZN’s saxagliptin (Onglyza) has struggled to gain share in the US, being overtaken by Lilly/Boehringer’s linagliptin (Trajenta) despite saxagliptin’s earlier launch.

**Figure 2: Comparison of US and UK Value Market Shares for DPP4 and SGLT2 Inhibitors**

![Graph showing comparison of market shares](https://example.com/graph.png)

*Source: Annual Reports and Evaluate Pharma – World Preview 2016, Outlook to 2022; PCA data from http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.asp*

**The UK Type 2 Market in more detail**

It is easy to pass off these phenomena as simply reflecting differential geographic marketing (and market access) strengths. However, there is little likelihood that the companies involved had forecast such skewed

\(^{2}\) AZN Q3 2016 Results Presentation
sales performances between markets so shareholders and management alike are entitled to ask why these deficiencies have not been addressed. Why has Janssen’s canagliflozin failed to take a reasonable share ex-US; why has AZN’s dapagliflozin not made greater inroads in the US; why is AZN’s saxagliptin a distant third in the UK DPP-4 market and why is Takeda’s alogliptin set to overtake AZN’s saxagliptin in the latter’s home market, despite a much later launch? These questions remain largely unanswered and suggest that future forecasts, including up to $150bn of cumulative sales to 2022, remain in doubt as to their company attribution.

In an attempt to unravel some of these questions we have started with the UK market and analysed publically available Prescription Cost Analysis (PCA) data to demonstrate how competitive advantage could be achieved. The UK may be small in relation to the US or German pharmaceutical markets but the same statistical principles apply to all. If one believes that freedom to influence demand is one of the inherent principles underpinning the success of the pharmaceutical industry as an important stakeholder in the healthcare ecosystem, then there should be no excuse for failing to implement accurate and robust data analysis in order to eliminate promotional waste and to deliver the clinical message.

**Figure 3: UK Market Position of DPP4 and SGLT2 Inhibitors May-August 2016**

![Figure 3: UK Market Position of DPP4 and SGLT2 Inhibitors May-August 2016](http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.asp)

Figure 3 plots the relative value market share (with MSD’s sitagliptin having a relative market share of 1.0) against growth rates of the DPP4 and SGLT2 inhibitors in the UK, using NIC data from publically available PCA from the NHS Business Services Authority. The time period examined is the “Tertial”, i.e. 4 month
period, from May to August 2016 compared with the same period the previous year. The size of the bubble for each product is an indication of total sales in the Tertial (see Figure 5 below).

**The underperformers identified**

As a general rule the first in class and best in class usually have a strong market position when the market has fully developed. MSD’s sitagliptin was first to market and is the market leader. More interesting is why AstraZeneca’s saxagliptin has been overtaken by Lilly’s linagliptin despite a two year launch advantage and is likely to be overtaken by Takeda’s alogliptin that has only been on the UK market for two years. It may be argued that positioning two oral drugs for Type 2 diabetes has confounded a clear marketing strategy; AstraZeneca have both saxagliptin and dapagliflozin. However, not only was there a three year gap between the launch of saxagliptin and dapagliflozin, allowing plenty of time for market positioning but Lilly/Boehringer Ingelheim have had no difficulty positioning linagliptin and empagliflozin, garnering strong market positions with both drugs.

A more compelling argument explaining AstraZeneca’s poor showing is the outcome of the SAVOR study that showed an increase in hospitalisation for heart failure when comparing saxagliptin with the placebo group. This was published in late 2013. However, Takeda’s alogliptin study, EXAMINE, also published in late 2013 showed a similar tendency. Indeed both alogliptin and saxagliptin have had FDA label changes as a result of these trials. Despite this Takeda continues to perform really well in the UK as a “tainted” latecomer. Takeda has launched alogliptin at a 16-20% discount to the other drugs in the class and this may override any safety concerns for price-sensitive customers. Nevertheless, there are serious questions to answer amongst the industry’s diabetes marketing teams.

**Figure 4: Launch success for selected DPP4 and SGLT2 inhibitors in England**

![Graph showing sales of different drugs](http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.asp)

Source: PCA data from http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.asp

Within the SGLT-2 class there are just three main products (plus combinations with metformin). See Figure 4. Although Janssen’s canagliflozin was not first to launch it could have expected a strong position if its US experience was any guide. However, AstraZeneca’s dapagliflozin has been the front runner, outselling canagliflozin by more than two to one. Despite being six months behind canagliflozin, Boehringer’s
empagliflozin has come out of the blocks quickly and has Janssen’s canagliflozin in its sights. The cardiovascular benefits have undoubtedly helped tell a good story but these benefits are still under consultation by NICE and are not scheduled for a scoping workshop until January 2017, despite being accepted by the European AdComm. It would be churlish to suggest that Janssen’s canagliflozin is a “loser” in this category and yet its UK market position contrasts strongly with that in the US and is also reaching a plateau with respect to penetration of GP practices (see Figure 7), an early warning sign perhaps of the slowdown to come.

**Figure 5: England Sales (based on NIC) for Key DPP4 and SGLT2 Inhibitors**

![DPP4/SGLT2 Inhibitor Sales and Growth Rates in England (May-Aug 2016 v Prior Year)](image)

Source: PCA data from http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.asp

From the outsider’s perspective there are two clear product outliers in terms of performance relative to expectation, given the scale of the commercial organisations behind them and the resources available; AstraZeneca’s saxagliptin and Janssen’s canagliflozin.

1/ Why is AstraZeneca’s saxagliptin now in decline and being out-sold three to one by Boehringer’s linagliptin and about to be overtaken by Takeda’s latecomer, alogliptin, in AZ’s home market?

2/ Why has Janssen’s canagliflozin, which is the clear market leader in the US, been outsold two to one by AstraZeneca’s dapagliflozin and likely to be overtaken by Boehringer’s empagliflozin in 2017?

**Some suggested further analysis**

As a first pass it is useful to see just where prescriptions of the Type 2 products are being generated and how they differ from GP practice to practice. A useful starting point is the sales split by SHA (Strategic Health Authority). The box plot in Figure 6 shows the variation in sales (as measured by Net Ingredient Cost) across GP practices by SHA. Key questions here are: Why is the variation in sales across SHAs so high? Is this simply reflecting population size, levels of diagnosis, levels of disease, KOL influence, brand vs. generic prescribing, formulary recommendation or other influences? It would also be helpful to know how
are Key Account teams doing in the various SHAs? What does success look like? Can it be explained by certain strategies or behaviours? Answering these questions would go a long way to understanding the healthcare ecosystem in which Type 2 diabetes products are prescribed and how field forces are faring.

**Figure 6: Sales variation of DPP4 and SGLT2 inhibitors across GP practices, split by strategic health authority**

![Sales variation across practices by SHA](image)

Source: PCA data from [http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx](http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx)

The next level of analysis could cut the prescribing data according to GP practice, allowing one to raise a series of additional questions. What are the characteristics of practices with high levels of DPP4/SGLT2 usage? Do they prescribe more innovative products generally, are they younger doctors, older, have greater levels of intra-practice prescribing agreement, or even are more heterogeneous in their prescribing habits? Where does a particular product do well and where badly? Does my product lose out in price-sensitive practices, gain in dispensing practices, or vice versa? What are the characteristics of practices where a particular product does well, or badly? Finally, what are the sales reps doing in territories where GP practices have high levels of prescribing of a particular product? How does their strategy differ from those in less successful territories? How responsive are customers to different marketing channels? Do they respond well to digital contact, prefer face to face, need KOL endorsement, want the latest clinical data, like to talk to medical liaison, attend clinical conferences, like group events or prefer the personal touch? What is the optimal call rate?

An additional graph (Figure 7) shows the number of GP practices using each product. (the first three DPP4 inhibitors have been excluded, mostly since they were launched before the NIC data became publically available. In any case they are less relevant to this debate.) What seems clear is that the sales success of dapagliflozin and linagliptin to date has been based on penetrating a high proportion of all GP practices. The success of empagliflozin, despite being the most recently launched product, seems to reflect an increasing level of practice penetration, almost matching the penetration of Janssen’s canagliflozin. Indeed, the...
apparent stalling of canagliflozin with respect to the number of GP practices actually prescribing the product is somewhat worrying and may indicate that a new approach is required if the drug is not to peak much earlier and at a lower sales level than it should.

**Figure 7: Sales of selected DPP4 and SGLT2 inhibitors in England according to time since launch**

![Graph showing sales of DPP4 and SGLT2 inhibitors in England.]

**Conclusion**
The key to effective marketing is clear innovative positioning and creative segmentation – two processes made especially potent by superior analysis and insight of marketing data. Alas in many cases CRM systems tend to “dumb down data” to the average, while practices like outsourcing to a data warehouse hand your most valuable competitive asset to an external party.
The questions in the previous section highlight some of the opportunities open to the discerning and innovative marketer who seeks to ambush the future and set the rules of engagement rather than follow the worn out old seam of traditional marketing with declining returns.

All these questions can be answered using a combination of publically available data and data from the company’s CRM system. If you would like to find out more just email stewart@pharmaforensic.co.uk

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