DIABETICINVESTOR

"Make the Connection"

David Kliff, Publisher

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Feasibility of Automating Insulin Delivery for the Treatment of Type 1 Diabetes – Diabetes, Vol. 55, December 2006

Since the introduction of insulin pump therapy, the ultimate dream was to develop a closed loop insulin delivery system or artificial pancreas. This dream seemed to move a step closer with the introduction of continuous glucose monitoring systems. The dream took another step forward when Medtronic (NYSE:MDT) introduced their Paradigm 722 – which combined the Paradigm 715 insulin pump with the Guardian RT continuous glucose monitor. It seems as though the dream, so long in coming, is about to become a reality. Medtronic has publicly stated that they hope to have the first semi-closed loop system available in 2008; a system which many believe will be the predecessor to a completely automated closed loop system.

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Feasibility of Automating Insulin Delivery for the Treatment of Type 1 Diabetes – Diabetes, Vol. 55, December 2006

Before everyone gets excited about what's supposed to be the next leap in the treatment of type 1 diabetes, it's time for a reality check. More appropriately, it's time to ask a fundamental question: Is a closed loop insulin delivery system truly possible or is it merely another pipedream? This may seem like a silly question when it seems we're so close to having just such a system. The reality is we're not as close as everyone thinks and are more likely further away than most insulin pump companies will let on. The facts are such that there are still many hurdles to overcome and not just technological, but structural also.

Before we examine this issue in detail, here's a quick overview of where we stand today:

1. Insulin pump therapy is widely regarded as one of the more effective treatments for type 1 diabetes.

2. A growing percentage of type 2 patients are adopting insulin pump therapy.

3. Although insulin pumps are medical devices and do experience mechanical failures, insulin pumps are regarded as safe.

4. Continuous glucose monitoring, although still in its early stages, is improving.

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5. Allowing an insulin pump to accept readings from a CGM is already here.

6. While the cost of insulin pump therapy can be significant, even for patients with full healthcare coverage, cost of insulin pump therapy is not generally considered an obstacle to therapy adoption.

7. Reimbursement is not generally an issue or impediment to therapy adoption.

8. There are five primary players in the insulin pump market:

Medtronic – 70-75% market share

Animas – a unit of Johnson and Johnson (NYSE:JNJ) - 14% market share

Deltec – a unit of Smiths Medical – 9% market share

Acc-Check (formerly Disetronic and now owned by Roche) – 4% market share

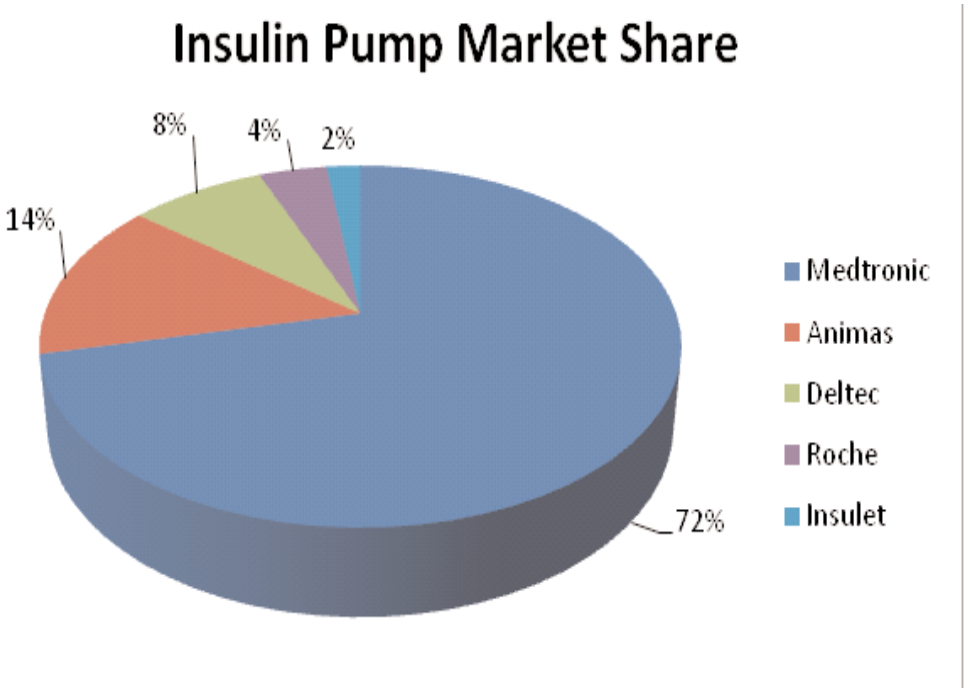
Insulet (NASDAQ:PODD) – 2% market share

9. Besides Medtronic, Dexcom (NASDAQ:DXCM) has an FDA approved CGM. Abbott (NYSE:ABT) is awaiting approval for their CGM and has an insulin pump already approved by the FDA but not currently on the market.

10. Diabetic Investor estimates the insulin pump market growing at 10% annually.

Now, let us explore the obstacles to seeing a closed loop insulin delivery system move from dream to reality.

So we are clear, Diabetic Investor defines a closed loop insulin delivery as a system that does not require any patient intervention other than maintaining the system, calibrating the CGM component and refilling the insulin. All dosing decisions are performed by the system. In effect, a closed loop system and artificial pancreas are one and the same. The difference between a closed loop and semi-closed loop system is in a semi-closed loop system there is patient interaction with the system. While the system may recommend dosing amounts, the patient can reject recommendations. For the record, Diabetic Investor believes a semi-closed loop system is ultimately doable and will be on the market in next year to 18 months.



Source: Diabetic Investor

First, let's look into the technological barriers:

According to the MAUDE database from January 1, 2007 to October 31, 2007, there were 100 deaths reported for patients using an insulin pump. It would be foolish to believe that in each incidence the insulin pump was responsible for the patient's death; it would be equally naïve to believe that there are not serious consequences when a pump malfunctions. While it is true that insulin pumps are generally safe, vast improvements will be needed when dosing decisions will be made without patient intervention.

Diabetic Investor has been critical towards Medtronic over the way they have handled the class II recall of the Paradigm pumps. After acomprehensive review of the MAUDE database, Diabetic Investor could not find one incidence of a pump failure that mentioned MRI other than pumps from Medtronic. It was noted in the recall that should a Paradigm pump come into contact with an MRI, there was the possibility that the pump could over deliver insulin which in turn could lead to a severe hypoglycemic event. Hypoglycemia is a serious and life threatening event.

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Photo courtesy of Medtronic

We have stated that there is a design flaw with the Paradigm line of pumps as no one failure should cause the pump to over deliver insulin. After interviews with other pump manufacturers, Diabetic Investor discovered that other pumps shut down when they violate pre-programmed protocols and do not allow the possibility for the over delivery of insulin. Although it was never directly stated, it appears these companies believe that although hyperglycemia is not preferable, it is easily treatable. In fact, the majority of insulin pump patients are equipped with syringes in the event their pump does malfunction. Experienced pump patients know that pumps do fail and are prepared for just such an event.

The point here is simple, pumps are machines and machines fail. Everyone has experienced a computer or cell phone failure at one time or another. While this is an inconvenience, it normally won't kill the user of the technology. Should a pump fail and begin to over deliver insulin, this could have drastic consequences.

Besides the pump working properly, the same concern surrounds CGM technology. Granted, we are still in the early stages of this technology, but the early results are hardly encouraging. Missed readings, failed sensors, sensors that don't calibrate, readings that do not correlate, etc. For a closed loop system to ever become a reality, the CGM component must work 24x7x365 without failure and provide highly accurate readings. What would happen if, for whatever reason, the sensor indicates the patient is at 240 when they are really at 100? The fact is sensor technology is the primary obstacle to a closed loop system ever becoming a reality. After interviewing several experts with years of CGM experience, not one believes that such a sensor will be available in the next 15 years and there are some who don't think there will ever be such a sensor.

The fact is, as advanced as both insulin pump and CGM technology have become, it is still not to the point where it is reliable enough to take control of insulin dosing decisions. But technology is just one obstacle to the dream becoming a reality. There are structural obstacles, too.

Diabetic Investor has interviewed several noted physicians, many of whom are strong advocates of insulin pump therapy. Almost universally, these physicians are uncomfortable putting dosing decisions in the hands of a machine, regardless of how good the technology is. The general consensus is that a semi-closed loop system that allows for patient intervention stands a greater chance for market acceptance. Since these physicians work with many insulin pump patients as well as patients using

The Medtronic Paradigm® REAL-Time System, the first system to combine an insulin pump with a continuous glucose monitoring system. The MiniMed Paradigm 522 and 722 Insulin Pumps have a list price of $6,195. The optional starter kit for the continuous glucose monitoring components has a list price of $999.

With their huge market share and extensive intellectual property portfolio Medtronic is well ahead of the competition in bringing a closed-loop system to market. The company has publicly stated that a semi-closed loop system should go to the FDA for approval sometime in 2008.

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CGM, they have seen firsthand both the promise and the peril of this technology.

How would such a system know that the patient wants their levels to be outside normal ranges? Using my own situation as an example, how would such a system know that I am carb loading for an upcoming marathon run and want my levels higher than normal? Could the system correct itself during my run to automatically lower my basal rate or possibly stop delivery altogether should my levels begin to crash?

What would the system cost? As it stands today, pumps cost $6,000 or more and another $2,000 per year for supplies. Will insurers be willing to reimburse for a system that many believe will cost north of $10,000 in the first year alone? Given the continuing concerns over the rising cost of healthcare and renewed emphasis on cost containment, cost is a factor.

One has to question what the regulatory pathway would be for this system. The FDA has already admitted they are not equipped to deal with the complexity of many new devices. According to a report issued by the The Science and Technology Subcommittee of the FDA Science Board this November, " The development of medical products based on "new science" cannot be adequately regulated by the FDA.

Rapid changes in biological sciences and bioinformatics are exceeding the capacity of current FDA science capabilities to keep pace and adequately support the Agency's safety mission. The FDA lacks sufficient expertise to understand the impact of product use, to maintain ongoing currency with their evolution or to evaluate the sophisticated products produced. In addition, the FDA has no consistent strategy to acquire that expertise."

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Is there really a market for this system? It has been widely assumed that there is a demand for a closed loop system. According to Medtronic, less than 28% of type 1 patients and less than 1% of type 2 patients use insulin pump therapy. Although there have been numerous studies demonstrating the effectiveness of insulin pump therapy for both type 1 and type 2 patients, insulin pump therapy is still vastly underutilized. On several occasions, Diabetic Investor has outlined the obstacles to insulin pump therapy, most notably the amount of time and education a patient needs.

Diabetic Investor has also outlined several examples where companies believed that advanced technology would create demand. The blood glucose monitoring (BGM) is a prime example of the mistaken belief that advanced technology would expand a market. Over the past few years, we have seen several notable advancements with glucose monitoring; faster test results, alternate site testing and meters that do not require coding. Still, the majority of patients do not test as frequently as they should and worse there is a high percentage of patients who do not test at all.

The same is true in the insulin pump market. Insulin pump technology has improved dramatically over the years. Pumps now come equipped with bolus calculators, the ability to accept readings from a glucose meter and food databases. These new "smart pumps" are more patient friendly, making pump therapy easier for both the patient and physician. However, just as with the BGM market, all this advanced technology has done little to increase the usage of insulin pumps.

Diabetic Investor see a closed loop system much in the same way we see the market for CGM or inhaled insulin; that being said, there is a market here, just not a very big market. However, this does not change our overall view of the insulin pump market, nor do we believe having such a system would be a major advantage and actually could be a disadvantage. Running an insulin pump company has more to do with patient support than it does in developing sophisticated systems. Insulin pump companies must run their patient support services 24x7x365, a

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The OmniPod Insulin Management System from Insulet and The Seven™ System from Dexcom. Although the two systems do not yet work together there is wide speculation of a deal brewing between the two companies. While Insulet does have an existing agreement with Abbott to integrate the still un-approved Navigator with the OmniPod, Insulet has publicly stated they are free to pursue other arrangements. Diabetic Investor sees an OmniPod/Dexcom combination as a powerful combination that could give Medtronic serious competition.

Photos courtesy of Insulet and Dexcom

function that is not easily transferrable to the web. As hard as pumps have tried, the fact remains that when a pump patient is having a problem, they don't go to the company's web site for answers, they call tech support. Try to imagine the increased call volume and complexity of each call for a closed loop system. Is it a pump problem? Is it a sensor problem? The more sophisticated the technology, the more that can go wrong.

Recently, much has been made of the role technology plays in the lives of patients with diabetes. There is absolutely no question that technology has vastly improved the lives of millions of patients. However, even with all this advanced technology, the most telling of all the statistics related to diabetes is that nearly 75% of the patients with diabetes are not properly controlling their disease.

Sadly, it appears that too many of the medical device companies are using this sad statistic to justify their continued pursuit of even more advanced technology. One would think they would have learned from the past and realized that advanced technology by itself is worthless if there is no practical application of that technology.

As Alice Embree wrote, "America's technology has turned upon itself; its corporate form makes it the servant of profits, not the servant of human needs."

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