

Delivery by Design: Pens for Injectable Therapies

a report by

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Diabetes continues to increase at an alarming rate worldwide and is now a major cause of death, with mortality risk twice that for individuals without the disease.¹ Most people with type 2 diabetes are started on lifestyle change and oral antidiabetic agents that address one or more of the physiologic defects that lead to hyperglycemia. Type 2 diabetes is a progressive disease that results from a decline in β -cell function caused by decreased B-cell response and increased B-cell workload. Many, if not most, people with type 2 diabetes will eventually need treatment with insulin or one of the new injectable therapies such as an incretin mimetic like Exenatide or amylin mimetic like Pramlintide.

The landmark Diabetes Complications and Control Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) clinical trials have shown that microvascular complications can be delayed with intensive treatments to achieve near normal glucose control.^{2,3} However, a report from the American Association of Clinical Endocrinologists (AAACE) found that 67% of people with type 2 diabetes are not meeting their target A1C of <6.5%.⁴

Patients face the challenges of the progressive diabetes pathophysiology and additional barriers such as weight gain and hypoglycemia.⁵ Both weight gain and hypoglycemia contribute directly to poor quality of life in people with type 2 diabetes.⁶

Barriers to intensive treatment include 'clinical inertia' on the part of providers as well as resistance to insulin from patients. Clinical inertia exists for both endocrinologists and primary care physicians, but endocrinologists are somewhat more likely to start insulin in patients who are not meeting glycemic targets.⁷ In addition to weight gain and hypoglycemia, additional challenges to optimizing insulin treatment include:⁸

- patients' fear of injections; and
- feel that insulin therapy will disrupt daily activities and impact quality of life.

Pen devices for insulin were first introduced by Novo Nordisk in the late 1980s but growth in the pen market was quite small for many years. Pen use did not start to increase until results of DCCT were released but total pen use in the US is still well below that of most industrialized countries.⁹ Insulin injections by pen in the US is approximately 15% compared to 80–90% in Europe.

Hornquist and colleagues assessed quality of life issues by doing a follow-up study in outpatients with type 1 diabetes who switched from the standard syringe-and-vial method to multiple insulin injection therapy via pen devices. They found glycemic control to be stable in a majority of study participants. Participants indicated that insulin pens allowed for a more satisfactory quality of life compared with traditional insulin syringes.¹⁰ Other studies have also found that patients over 50 were able to use disposable prefilled pens with comparable blood glucose profiles to previous glucose levels while using reusable pens. Patients expressed preference for prefilled pens over re-usable pens that had to be filled with cartridges of insulin.¹¹

In reviewing numerous studies, K E Robertson and colleagues conclude that pen devices are an acceptable method insulin delivery and patients often prefer using pens over traditional syringe-and-vial. Glycemic control with pen devices is comparable to that of standard insulin delivery devices in younger and older patients, in patients on traditional twice-daily injection schemes, and in patients treated with intensive multiple injection regimens.^{1,2} A new device coming on the market incorporates a memory feature in a reusable pen. The pen can replay the dates and times and doses for the previous 16 doses and this feature may be important to assist patients with catching missed doses quickly and avoiding 'stacking' insulin doses. Stacking the dose means taking a 'touch-up' dose after the meal to address a postprandial high glucose without taking previous doses into account. This results in hypoglycemia before the next meal, eating to catch up with the hypoglycemia, then going high... in other words the patient is 'chasing' his blood glucose throughout the day.

Some of the barriers to pen use in the US are provider issues and some are payer issues. Many providers are still unaware of the pen as an option and some consider pens a novelty or convenience item. In US centers with a high rate of pen use, pens are offered to all insulin-using patients. Given the option, most patients opt for a pen.⁹ Healthcare provider attitude toward injectable therapy represents an important influence on patient adherence. Patients who hold positive views regarding their therapy are far more likely to be adherent. Patients also report social stigma from giving injections in pubic and pen delivery devices can mitigate these concerns.¹³

Too often, pens are not covered by insurance because of the increased cost of pens over vials.⁹ The increased cost is minimal compared with other pharmaceutical approaches and the potential benefit from achieving glycemic targets proven to prevent or delay complications.

Addressing barriers to patient use of injectable therapies is critical to achieve success with glycemic targets. Some of the strategies include:¹³

- Assess patient beliefs and attitudes regarding the new

therapy being recommended. Patients often have misconceptions about the potential benefits and side effects of therapy and it is critical to identify these and arm the patient with accurate information.

- Provide self-management education on lifestyle strategies to address diabetes control issues and potential weight gain related to insulin use. Training by a diabetes educator can assure appropriate skills when using a new device and enhance adherence.

Offer a variety of options for delivery of insulin and empower the patient to acquire these with appropriate reimbursement. Reimbursement issues must be addressed by patients who demand this level of quality care from payers for this technology to become available in the US.

Achieving success with diabetes care requires a team approach. This team must include patients, providers, diabetes educators and payers to completely address the needs of the person with diabetes. Insulin delivery devices that provide simplicity, accuracy, discreet delivery, and improved quality of life should be considered for patients who require an injectable medication. ■

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