Device Profile

EXPERT REVIEWS

Insulin glargine and glulisine SoloSTAR® pens for the treatment of diabetes

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Insulin is an effective medication for lowering hemoglobin A_{1c} values and can be used for both basal and prandial coverage of hyperglycemia in Type 1 and Type 2 diabetes. Despite its effectiveness there is still reluctance by patients and physicians to add insulin into the treatment regimen for Type 2 diabetes when needed. One of the key barriers to initiating insulin therapy is the method of delivery. Insulin delivery pens are continually developed as a means to improve upon the vial and syringe and to make it easier for patients to incorporate insulin therapy into their lifestyles. The SoloSTAR® pen (Sanofi-Aventis, Paris, France) was developed to make insulin delivery easier and to help eliminate barriers to the initiation of insulin therapy. In this article, we discuss the features and characteristics of SoloSTAR that overcome existing unmet needs.

KEYWORDS: diabetes • hypoglycemia • injection force • insulin • insulin dose • SoloSTAR® pen

The increasing prevalence of diabetes in most populations has had a major impact on healthcare systems worldwide [1]. Global projections for diabetes are increasing at an alarming rate, with the total number of people with diabetes projected to rise from 171 million in 2000 to 366 million in 2030 [2]. In the USA for example, crude prevalence in 1999–2002 of total diabetes was 6.3% (19.3 million, 2002 US population), consisting of 3.5% diagnosed and 2.8% undiagnosed [3]. Currently, the prevalence of diabetes in the USA is approximately 7.0% (21 million people with diagnosed or undiagnosed diabetes) [101]. This rise in prevalence of diabetes is closely associated with an increasing prevalence of obesity across the globe (FIGURE 1) [2,4,5,102,103].

In healthy individuals, pancreatic β cells respond to changes in blood glucose by secreting insulin and increasing insulin synthesis. Diabetes is characterized by progressive β-cell failure, resulting in a decline in insulin secretion and hyperglycemia [6]. The therapeutic approach to diabetes commonly involves intensive insulin management (basal/bolus) to maintain normal glycemic levels, by replacing insulin as close to the physiological insulin secretion profile of healthy individuals as possible [6]. For patients with Type 1 or Type 2 diabetes, maintaining glycemic levels as close to the nondiabetic range as possible has been demonstrated to reduce the risk of developing diabetes-specific complications, including retinopathy, nephropathy and neuropathy [7–9]. Insulin is the most effective diabetes medication in lowering glycemia and, when used in adequate doses, can decrease any level of elevated hemoglobin (Hb)A_{1c} [10].

The recently published American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) consensus statement guidelines recommend the early addition of insulin therapy in patients who do not meet target goals (BOX 1) [10].

Previous data from intermittent self-monitoring of blood glucose (SMBG) in Type 2 diabetes indicated higher contributions to elevated HbA_{1c} from fasting blood glucoses at higher levels (>9%), and significantly higher contributions to rise in HbA_{1c} from postprandial blood glucose (PPBG) at lower HbA_{1c} levels (<8%). More recent data from continuous glucose monitoring (CGM) systems indicate an inability for patients to achieve normal fasting blood glucose, even amongst those with near normal HbA_{1c} values (i.e., <6%; FIGURE 2) [11]. In addition, a significant contribution to rises in HbA_{1c} levels also comes from post-dinner elevations in blood glucose at higher HbA_{1c} values, which in turn might contribute to higher fasting blood

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glucose levels. Glucose variability, in part due to postprandial hyperglycemia, has been demonstrated to correlate with oxidative stress markers [12]. Recent data from CGM also indicates loss of postprandial glucose control preceding fasting hyperglycemia with increasing duration of diabetes (FIGURE 3) [13]. Thus, early focus on postprandial hyperglycemia may need to be considered (across all HbA_{1c} levels), especially when attempting to achieve normal fasting glucose.

Overview of the market: the impact of glucose control

Tight blood glucose control has been shown to prevent, or delay, the development of diabetes-related microvascular and macrovascular complications. An epidemiologic analysis of data from the United Kingdom Prospective Diabetes Study (UKPDS) patient population demonstrated that for each 1% reduction in mean HbA_{1c}, there was a 37% reduction in risk for microvascular complications alongside a 14% reduction in macrovascular complications [14]. Similar data from the Diabetes Control and Complication Trial (DCCT) in Type 1 diabetes shows the benefits of intensive insulin therapy resulting in significant reductions in both microvascular and macrovascular complications. Despite all of the available data, only approximately 30% of patients with Type 2 diabetes are on some sort of insulin treatment in the USA [15,101]. While this is, in part, due to some patients being well controlled with lifestyle management and oral antidiabetic drugs (OADs), patient and physician reluctance to start insulin therapy is also thought to be a contributor [16,17]. In order to achieve and maintain tight blood glucose control, insulin use in patients diagnosed with diabetes should be an integral component of their management strategy. Most patients with Type 1 diabetes, and increasingly more patients with Type 2 diabetes, use two different types of insulins to provide basal and prandial coverage for hyperglycemia; however, many still use premixed formulations. Indeed, it has been estimated that premixed insulins account for 22% of the total volume of insulin sold worldwide [15]. Premixed insulin usually contains a rapid-acting insulin and an intermediate-acting insulin with an aim to mimic endogenous insulin secretion patterns [18]. However, the use of premixed insulins is declining as the use of basal and prandial insulin increases [15], which is in line with the ADA/EASD consensus guidelines that only recommend the use of premixed insulin after a patient is stabilized on insulin and if their mix ratio is close to one of the available premixed insulin ratios [10].

A basal insulin supply, such as insulin glargine (Lantus®; Sanofi-Aventis, Paris, France), which has a relatively constant and peakless delivery over 24 h [19], can provide the steady, low-level insulin that is constantly present in the circulation to cover preprandial and overnight fasting periods. This is supplemented with multiple preprandial injections of regular human insulin or rapid-acting insulin analogs, such as insulin glulisine (Apidra®; Sanofi-Aventis, Paris, France), which aim to normalize and maintain good glycemic control, reduced glucose variability and better HbA_{1c} values.

Box 1. Summary of the American Diabetes Association/European Association for the Study of Diabetes consensus algorithm for the management of Type 2 diabetes.

- Step 1. Lifestyle modification and meformin
  - Lifestyle modification and metformin at diagnosis
  - Titrate metformin to maximum effective dose over 1–2 months
  - Check HbA_{1c} every 3 months until <7%, and every 6 months thereafter
- Step 2. Intensify therapy
  - Add further medications within 2–3 months if HbA_{1c} remains >7%:
    - Insulin
    - Sulfonylureas
    - Glitazones
  - Choice of agent depends on HbA_{1c} level
  - Insulin is recommended if HbA_{1c} remains >8.5%

HbA_{1c}: Hemoglobin A_{1c}.
From [10].

Insulin administration

An important aspect of diabetes care and glycemic control is the delivery of insulin. The method by which insulin is administered has been shown to impact patient acceptability of insulin therapy and quality of life, and may serve as a key barrier to insulin initiation [20]. Previously, the predominant route of insulin administration for patients with diabetes was the syringe and vial. However, this method of administration has many disadvantages, including fear of injections [21,22], poor dose accuracy [23], lack of social acceptance [24], inaccuracy when self-mixing insulins [25] and possibly changing pharmacokinetics of both long- and rapid-acting insulins. While still an injection device, insulin pens help to overcome many of these barriers.

Since the introduction of the first insulin pen, NovoPen® (Novo Nordisk, AS Bagsvaerd, Denmark) in 1985, insulin pens have continued to improve in design and usability features and address many of the barriers associated with administering insulin using a syringe and vial. Precision and accurate dosing is crucial for patients with diabetes, particularly for those on complex treatment regimens. Previous studies have indicated that up to 80% of people with diabetes incorrectly administer their insulin when using a syringe [26,27]. Santiago *et al.* conducted a precision, accuracy and durability study of an insulin pen (NovoPen) that tested the pen at three preset doses under stress conditions (multiple thermal and vibration stress tests), which were intended to replicate daily use by patients [28]. The accuracy of the insulin pen was within 1% of the preset dose after the stress and endurance tests, and the precision of the pen devices were likewise high (delivery-dose relative error was at most 0.8% of the intended dose) after thermal stress, vibration stress, free-fall testing or 5-year endurance testing.

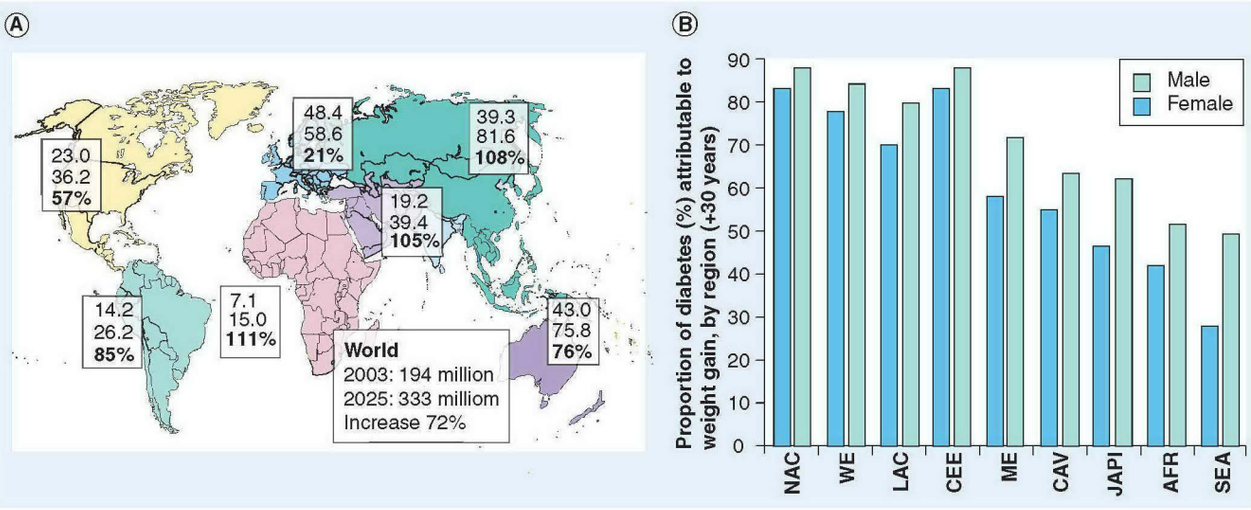

Figure 1. (A) Global projections for the diabetes epidemic; 2003–2025 (millions) and (B) increasing prevalence of obesity.
AFR: Africa; CAV: China and Vietnam; CEE: Central and Eastern Europe; JAPI: Japan, Australia and Pacific Islands; LAC: Latin America/Caribbean; ME: Middle East; NAC: North America/Cuba; SEA: South-East Asia; WE: Western Europe.
Part **(A)**: Reprinted with permission from Macmillan Publishers Ltd [1].
Part **(B)**: Information from [2,4,5,101,102].

Korytkowski *et al.* demonstrated that 82% of patients (n = 105) indicated greater confidence with dose setting using FlexPen® (Novo Nordisk) versus 11% of patients who preferred the syringe and vial method [29]. In addition, it was also demonstrated that 73% of patients reported more confidence in the accuracy of the dose delivered with FlexPen compared with 19% of patients using a syringe and vial. Insulin pens are now the predominant form of insulin administration in many countries, accounting for over 50% of insulin use worldwide, especially in Europe and Asia. In the USA uptake of insulin pens is steadily increasing, but it lags behind that seen in Europe and Asia [30].

Unmet needs

While insulin pen devices have made it easier for users to administer insulin, there remains scope for further development of insulin pens in response to unmet patient needs in relation to the development of SoloSTAR® (Sanofi-Aventis). Type 2 diabetes is characterized by obesity and insulin resistance and, coupled with the progressive nature of the disease, increasing doses of insulin are required over time. Accordingly, many patients need to administer doses of insulin exceeding 60 units, the maximum dose of many insulin pens, thus necessitating multiple injections. Limited joint mobility of the hand, commonly referred to as cheiroarthropathy, is frequently observed in patients with diabetes, particularly elderly patients, and is characterized by low grip strength and/or limited dexterity [31,32], which can impede the efficient administration of insulin, in such patients, using pen devices.

Problems with visual acuity are common in patients with diabetes and occur primarily as a result of diabetic retinopathy [33,34]. People with diabetes, particularly those with Type 1 diabetes, often use more than one type of insulin to manage basal and prandial insulin requirements, which can be provided by insulin glargine and insulin glulisine, respectively. The doses and pharmacodynamics of prandial and basal insulins differ; accordingly, it is important that the delivery devices are sufficiently differentiated to ensure low risk of users confusing the two insulin formulations. Patients with visual problems also place a greater reliance on non-visual modes when selecting dose. Dose setting and injections can be aided by audible recognition (the click sound), which occurs when a dose is dialed [35].

The SoloSTAR pen

An overview of the SoloSTAR pen & how it works

The continual evolution of insulin devices has led to the SoloSTAR pen, which is a prefilled, disposable insulin pen device designed for use once or several times daily. It is available for the administration of basal insulin glargine and prandial insulin glulisine for patients with either Type 1 or Type 2 diabetes, with two colors to differentiate the two pen devices. The insulin glargine SoloSTAR pen is approved for use in both the EU and the USA, whilst the insulin glulisine pen is approved for use in the EU.

The SoloSTAR pen is very easy to use. The user checks that they have the correct insulin pen. The user then attaches a new pen needle and performs a safety shot of 2 units to verify that the needle is working. The user then dials their dose and delivers the dose subcutaneously by pressing down on the injection button. The user will then remove the pen after counting to ten at the end of the injection to ensure the full dose is delivered. The needle is then taken off the pen and discarded safely. The pen cap is replaced and the pen can be stored until the next use. New, unopened

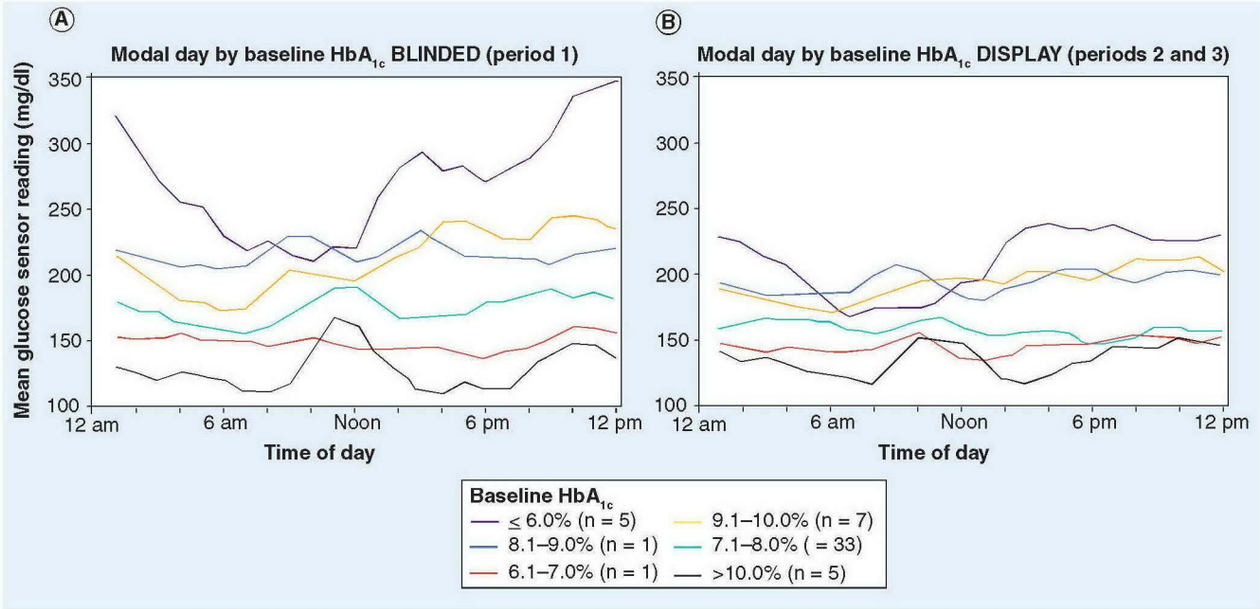

Figure 2. Modal day by baseline HbA_{1c} while subjects were blinded (A) to continuous glucose data or while subjects were given real-time access to continuous glucose values (B), trend graphs and high/low alerts.
Significant postpradial elevations in blood glucose levels were observed across all HbA_{1c} levels in both periods.

SoloSTAR pens should be kept in the refrigerator (2–8°C). Once opened, the SoloSTAR pen should be kept at room temperature for up to 28 days in accordance with storage condition recommendations, which differ in the EU (recommendations being below 25°C) and US (being below 30°C).

Evaluation of the SoloSTAR pen & responding to unmet needs

The SoloSTAR pen builds upon the strengths of current devices while including additional features, which have been ergonomically tested in order to establish their usability and effectiveness. Testing included collection of anthropometric data in intended user populations in order to recommend the most suitable user dimensions of the pen and develop the strength and robustness of the SoloSTAR pen, which compliments its user population.

Sensitivity & specificity

During development of the SoloSTAR pen, human factors were also considered, which led to a short-dial extension design facilitating easier grip during injection and enabling the user to administer even the maximum insulin dose with ease. This is an essential feature of the SoloSTAR pen when taking into account cheiroarthropathy, which is a significant problem in some patients with diabetes [31,32], with estimates that up to 58% of patients with diabetes have limited joint mobility of the hand [36] and significantly lower-grip strength compared with healthy controls [37]. The SoloSTAR pen has a maximum dose administration of 80 units, which exceeds the maximum dose of other available pens, except OptiClik (also 80 units), but including FlexPen and Lilly pen, which both administer a maximum of 60 units (Table 1). With higher doses of insulin required in obese patients especially with Type 2 diabetes, this is an important feature of the SoloSTAR pen, as it enables higher dose users to minimize the number of injections required.

Also, under varying temperature conditions, the SoloSTAR pen successfully passed dose accuracy testing, ensuring consistent and reliable insulin dose accuracy in a laboratory setting (Table 2) [38]. Moreover, the measured dose accuracy of SoloSTAR, when used by patients in a clinical setting, was within the limits of the International Organisation for Standardisation dose accuracy standard [39]. This reassures patients that, when used correctly, the SoloSTAR pen will deliver the dialed dose, which facilitates the titration of insulin dose without an increased risk of hypoglycemia or hyperglycemia. Injection force testing was performed to measure the force and force characteristics required to dispense a known volume of insulin (40 units) within a 4-s time period (Table 3) [38]. Findings from these tests showed that the SoloSTAR pen's highly efficient drive mechanism translates into a lower injection force than that of the Flexpen and Lilly pen [38].

To facilitate the differentiation of the insulin glargine pen from the insulin glulisine pen and to avoid the mistaken administration of basal instead of prandial insulin, or vice versa, the SoloSTAR pen is manufactured in two different

Table 1. Features of the SoloSTAR®, FlexPen® and Lilly pen.

Device	Maximum dose (units)	Dose increments (units)	Insulin products that can be administered using each pen*
SoloSTAR® (Sanofi–Aventis)	80	1	– Insulin glargine (LANTUS®) – Insulin glulisine (Apidra®)
FlexPen® (Novo Nordisk)	60	1	– Insulin detemir (Levemir®) – Insulin aspart (NovoLog®) – NPH insulin (Insulatard®) – NovoMix® 30 (30% insulin aspart and 70% protaminated insulin aspart)
Lilly pen (Eli Lilly and Company)	60	1	– Insulin lispro (Humalog®) – NPH insulin (Humulin®) – Humalog Mix75/25™ (75% insulin lispro) protamine suspension, 25% insulin lispro) – Humalog Mix50/50™ (50% insulin lispro protamine suspension, 50% insulin lispro)

*Availability may vary.
NPH: Neutral protamine Hagedorn.

colors: grey for insulin glargine and blue for insulin glulisine. This makes the SoloSTAR pen the first disposable insulin pen device to differentiate in pen body color.

This feature was included after consultations and assistance from healthcare providers, who suggested it to further minimize any confusion between the two insulins, especially in patients with visual impairments (Figure 4). In addition, another difference between insulin glulisine and glargine SoloSTAR pens includes a tactile differentiation of a raised ring on the dose button of the insulin glulisine pen, and other differentiation features include different colors in the labels and packaging.

Cost–effectiveness

Results from a recent study demonstrated that, in patients with Type 2 diabetes treated in a managed care setting, conversion from insulin injection with a syringe and vial to administration with an insulin analog pen device was associated with significantly lower annual treatment costs (US$16,359 vs 14,769, respectively; $p < 0.01$) as a result of improved medication adherence, fewer hypoglycemic events and reduced emergency department and physician visits [40]. These reductions could be as a result of the increased accuracy in dosing and timing of injection when using the insulin pen, which leads to a lower risk of hypoglycemia. Medication adherence was significantly improved after conversion to the insulin pen device (from 62–69%; $p < 0.01$).

A further potential cost saving for direct treatment could be made using pens when considering that insulin in vials is discarded by physicians after 28 days as per US FDA guidelines. Accordingly, insulin pens could be more cost effective for children and those taking small amounts of insulin. Since each insulin pen only contains 300 units, there will be less wastage, maintainance of biological activity of insulin and greater likelihood to follow the FDA label in clinical practice.

Recent results on the usability of the SoloSTAR pen reported by 65 healthcare professionals in clinical practice consider the SoloSTAR pen to be both easy to teach and easy to use for people with diabetes [41]. Of 65 healthcare professionals interviewed, most (n = 52; 80%) were able to spend less than 10 min training their patients to use SoloSTAR. This ease of use for both patients and healthcare professionals can translate into significant cost savings in relation to the time and resources spent training users of the SoloSTAR pen.

Use of the SoloSTAR pen in in-patient/hospital settings

In an in-hospital setting, the accuracy of the dose delivered is a key factor when selecting an insulin delivery system. This is because lack of accuracy may increase the risk of hypo- or hyperglycemia, jeopardizing patient welfare and in turn increasing diabetes-related treatment costs [38]. Used correctly, SoloSTAR pens will accurately administer the dialed dose of insulin, allowing reliable dose adjustment and minimizing the risk of resulting hypo- or hyperglycemia. In addition, color differentiation of the insulin glargine and glulisine SoloSTAR pens reduces the potential for hospital staff to confuse the two devices [38]. Furthermore, due to the ease of use, the introduction of insulin therapy in the hospital setting is easier with SoloSTAR pens than with traditional syringes and vials and this may result in patients being more likely to continue insulin therapy when discharged from hospital [38].

Clinical profile & post-marketing findings

Haak *et al.* recently conducted a preference study across four countries (US, Germany, France and Japan) involving 510 patients with Type 1 and Type 2 diabetes investigating the usability of the SoloSTAR pen, FlexPen and Lilly pen [42]. Patients were assessed on their ability to correctly perform a number of tasks involved in using each pen (including getting started and removing the cap, attaching a needle, setting and delivering a safety dose and dialing and delivering a 40-unit dose) and their preference of pens. The assessed steps for the SoloSTAR pen and FlexPen devices were correctly completed by a similar proportion of patients: 94% for the SoloSTAR pen

Table 2. Dose accuracy of the SoloSTAR® pen device (insulin glargine) at dialed doses of 1, 40 and 80 units at temperatures of 5°C, ambient temperature (18–28°C) and at 40°C.

Dialed dose	1 unit	40 units	80 units
Recommended range according to ISO standards	0–2	38–42	76–84
Cool temperature (5°C)	1.22 ± 0.18	39.85 ± 0.28	79.75 ± 0.29
Ambient temperature (18–28°C)	1.09 ± 0.15	39.92 ± 0.34	79.82 ± 0.28
Hot temperature (40°C)	1.15 ± 0.11	39.87 ± 0.11	79.73 ± 0.14

Results are means ± standard deviation; 30 pens were used for each dose, with two replicates per pen.
ISO: International Organisation for Standardization.

and 90% for FlexPen; however, fewer patients correctly completed the same steps with the Lilly pen (61%). When patients were asked to rate their preference for each pen based on various usability features, the feature 'easy/intuitive to figure out' was rated as 'best' most frequently for the SoloSTAR pen (55% of the time) followed by FlexPen (32% of the time) and least frequently for the Lilly pen (13% of the time).

Similar findings were also observed in the usability subgroup analyses based on age, previous pen experience and visual/dexterity disabilities. A high proportion of patients aged 60 years or over correctly completed the assessed steps with the SoloSTAR pen (90%) and FlexPen (83%) compared with the Lilly pen (47%). A high proportion of patients with dexterity (91%) and visual (94%) impairments correctly completed all steps analyzed with the SoloSTAR pen, which was similar to that observed with FlexPen (84% of patients with dexterity and 89% of patients with manual impairment). Only half of all patients with either dexterity (52%) or visual (52%) impairments correctly completed all analyzed steps with the Lilly pen.

The ease of use of SoloSTAR has also been demonstrated in a single-center, open-label, single-arm sequential study, which investigated the usability of the SoloSTAR pen by patients with Type 1 or Type 2 diabetes, aged 21–78 years [39]. After either face-to-face training (Part 1) or self-training (Part 2), subjects performed three dose-delivery repetitions into an injection pad using separate pens; pens were weighed before and after each dose delivery. The primary end point was the proportion of subjects delivering successful doses with all three repetitions. In Part 1, all 50 subjects delivered successful doses (100% success rate; 95% lower confidence bound [LCB]: 94.2%) and was within the limits of the ISO dose accuracy standard. In Part 2, 53 out of 54 validation subjects delivered successful doses (98%; 95% LCB: 91.5%). This study validates the SoloSTAR pen device for use by people with diabetes, with or without face-to-face training and showed that the SoloSTAR pen accurately delivered the dose that was dialed.

In order to determine the usability and safety of the SoloSTAR pen in clinical use, a 3-month observational study of 2029 participants (1067 with Type 1 diabetes and 926 with Type 2 diabetes) was undertaken, with the primary end point defined as absence of serious adverse events directly related to a validated technical failure of the pen. Eight product technical complaints (PTC) were investigated and most were due to handling errors. In total, 62 participants reported 77 adverse events, none of which were related to a PTC. Overall, most (95.4%) patients reported that they were either 'very satisfied' or 'satisfied' with the SoloSTAR pen, and 96.8% of patients continued to use SoloSTAR at the end of the study [43].

How does the SoloSTAR pen fit in the current treatment of diabetes?

With evidence from the DCCT [7] and UKPDS [8] studies indicating that improving glycemic control in patients with either Type 1 or Type 2 diabetes delays the onset of microvascular and macrovascular complications, intensive insulin treatment as a means of achieving and maintaining glycemic control has increased. The availability of the SoloSTAR pen for basal (insulin glargine) and bolus (insulin glulisine) insulin provides both clinicians and patients alike with a simple approach for managing diabetes. With the gradual progression of Type 2 diabetes, the ADA recommend lifestyle approaches, including nutrition and exercise, as important components of diabetes management followed by the introduction of one or more OADs, particularly metformin or sulfonylurea [44]. In addition to the aggressive approach for achieving target HbA_{1c} levels of less than 7.0%, step two of the ADA recommended treatment pathway (Box 1) now includes basal insulin, such as insulin glargine, as an option. Also, if HbA_{1c} levels are above 8.5% with a first-line approach, it is wise to move to insulin therapy as additional oral medications are not likely to achieve target HbA_{1c} values.

This concept is supported by a wealth of clinical data, including trials such as the 36-week Lantus and Metformin (LANMET) study, comparing with NPH and metformin in Type 2 diabetes, conducted by Yki-Jarvinen *et al.* [45], which demonstrated that the early introduction of insulin glargine (with adequate titration of dose) to one OAD improved glycemic control with a low risk of hypoglycemia (during the last 12 weeks of this study, fasting plasma glucose [FPG] averaged 5.75 ± 0.02 mmol/l and mean HbA_{1c} was 7.14 ± 0.12%). The next step in the treatment pathway should be the introduction of one prandial dose of insulin, such as insulin glulisine. A recent study on the basal plus approach demonstrated that the addition of insulin glulisine at breakfast or the main meal, for patients with Type 2 diabetes allows more patients to reach target HbA_{1c}, while offering patients a flexible injection time (insulin glargine can be administered immediately after a

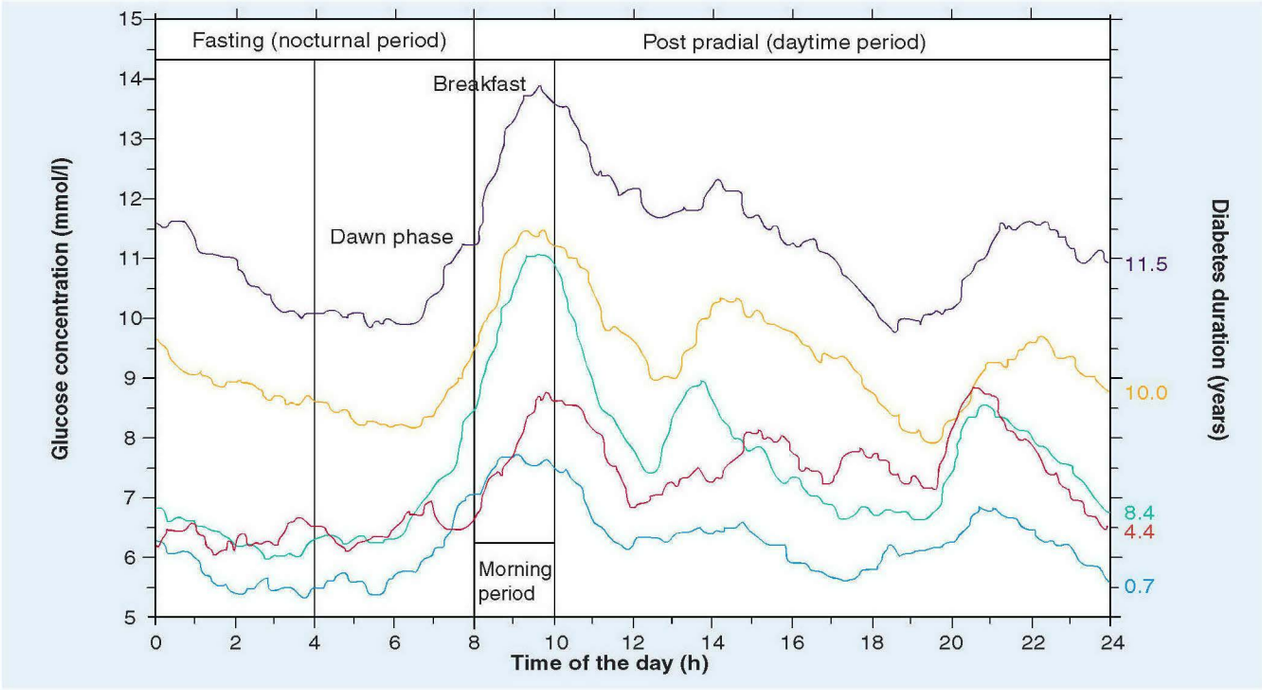

Figure 3. The 24-h recordings from continuous glucose monitoring in people with Type 1 diabetes.
Curve 1 (blue): HbA_{1c} < 6.5%; curve 2 (red): 6.5 to <7%; curve 3 (green): 7 to <8%; curve 4 (orange) 8 to <9%; curve 5 (purple): ≥ 9%. With increasing duration of Type 2 diabetes, post-prandial glucose elevations precede rise in fasting blood glucose levels.

meal, if necessary) [46]. This then offers a platform on which further prandial doses can be added, if patients are not reaching target [47]. Patients using the SoloSTAR pen would benefit from not having to undertake additional learning to use a different type of pen when adding prandial insulin to their existing basal insulin regimen, and the different colors and tactile features mean that patients are at a low risk of confusing their insulin pens.

The low injection force with SoloSTAR compared with FlexPen and the Lilly pen [38] may offer advantages, particularly for people with limited manual dexterity, which may be age-related or as a result of other complications [31,32]. In the study by Haak *et al.* [42], 81 participants had dexterity impairments; of these 91% of participants completed a dose delivery with SoloSTAR versus 84% with FlexPen and 52% with the Lilly pen.

Two devices, the Autopen® (Owen Mumford, Ltd, Oxford, UK) and Innolet® (Novo Nordisk), both have low injection forces, thus making them potentially suitable for people with limited dexterity. Autopen is differentiated by body color and is a reusable cartridge-based pen, while the Innolet has a large dose dial, with color differentiation on the injection button. However, the maximum doses that can be injected by Autopen and Innolet are 42 and 50 units, respectively. SoloSTAR fulfils the needs of these people, offering a higher maximum dose, color differentiation and low injection force, which means it could also be used by people with limited dexterity. Nevertheless, studies are of interest to evaluate the use of SoloSTAR in this patient population as well as in people with limited visual acuity.

Conclusions

The method by which insulin is administered has been shown to impact patient acceptability of insulin therapy and quality of life, and may serve as a key barrier to the initiation of insulin. A number of criteria should be considered when identifying the ideal insulin pen, including ease of use and ease of learning how to use the device. The SoloSTAR pen fulfils these criteria, as well as having an increased maximum dose and lower injection force than its competitors. Dose accuracy is also a core aspect of an insulin pen's function, and the SoloSTAR pen has successfully passed a number of dose accuracy tests. Thus, demonstrating that SoloSTAR pens are very accurate, consistently delivering the dialed doses of insulin within the specifications of the ISO standards. Alongside these benefits, the SoloSTAR pen facilitates the differentiation of the insulin glargine pen from the insulin glulisine pen by being manufactured in two different colors, with tactile differentiation. Here we present data verifying that the SoloSTAR pen provides a simple and more convenient method to administer insulin compared with a syringe and vial, and may help address many of the barriers to insulin therapy in patients with diabetes.

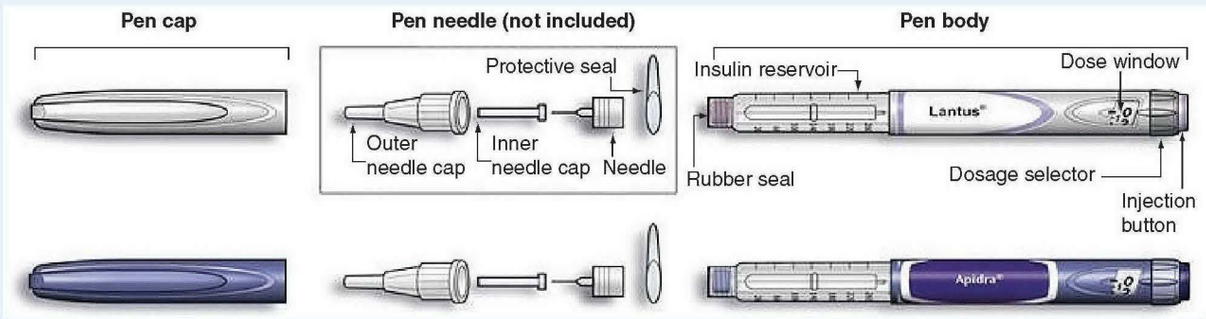

Figure 4. The SoloSTAR® pen device showing key components of the pen and needles and the color schemes used to help differentiate between insulin formulations.
Reproduced from [38], with permission from Informa Healthcare.

Expert commentary

Pen devices have reduced some of the anxiety and stress associated with initiating insulin therapy for many patients, which is attributable to their ease of use and ease with which they are incorporated into modern lifestyles (more portable and socially acceptable than the syringe and vial). If patients feel more comfortable with their insulin administration devices, the likelihood of adherence to insulin therapy is increased, as demonstrated by Lee *et al.* in their medication adherence and health economics study of patients with diabetes converting to insulin pen therapy from the syringe and vial (treatment adherence increased significantly after conversion to insulin pen therapy; $p < 0.01$) [40].

The SoloSTAR pen meets a number of previously unmet needs. The features of the SoloSTAR device, including its high dose capacity, reduced injection force, simplicity of use and different color scheme and tactile features for insulin glargine and insulin glulisine, make the SoloSTAR pen suitable for a wide range of patients with diabetes, particularly those taking both basal and prandial insulin, and for patients with visual or dexterity disorders.

Five-year view

As the number of patients treated with insulin continues to grow, there is a need for simple, effective insulin regimens that require minimal time and effort to educate patients in insulin administration. The ease and simplicity of the SoloSTAR pen helps to instill confidence in the patient, thus promoting regimen adherence and better glycemic control. Rhee *et al.* demonstrated that patients with an adherence rate greater than 75% had a decrease in HbA_{1c} from a baseline value of 9.1–7.8% after 12 months [48]. In addition to the benefits in terms of patient preference and convenience of handling, switching from vial and syringe to an insulin pen may reduce the occurrence of hypoglycemia [40] and, therefore, lead to a reduction in the fear of hypoglycemic episodes, thus leading to better adherence and

Table 3. Comparison of injection forces between SoloSTAR®, FlexPen® and Lilly pen.

Pen	Insulin	Mean force for total dose (N)	Mean plateau dose force (N)	Peak dose force (N)	Mean peak plateau dose force (N)	Peak priming force (N)
SoloSTAR®	Insulin glulisine	10.3	12.0	14.2	12.6	18.7
	Insulin glargine	11.3	13.4	15.2	13.9	17.4
FlexPen®	Insulin detemir	16.3	18.3	23.9	21.2	22.6
	Insulin aspart	17.2	19.2	25.5	22.7	23.8
	NPH insulin	17.7	19.9	25.5	22.8	21.7
Lily pen	NPH insulin	24.4	28.0	30.7	28.3	24.4
	Insulin lispro	25.3	28.8	32.9	29.2	26.6

Each pen was set to deliver one 10-unit dose to prime the pen, before delivering three subsequent doses of 40 units each.
N: Newton; NPH: Neutral protamine Hagedorn.

tighter glycemic control. Although not yet demonstrated with the SoloSTAR pen, it is conceivable that greater adherence, as well as better strategies for management of diabetes, will improve health outcomes. Forthcoming studies are underway to further evaluate the impact of the SoloSTAR pen on medication adherence and associated clinical and economic outcomes. Future developments in technology must include memory capabilities in the SoloSTAR pen without increasing the size of the devices.

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Key issues

- The global prevalence of diabetes is steadily increasing and is expected to exceed 330 million people in 2025.
- Insulin therapy is essential in Type 1 diabetes and is becoming more commonly used in Type 2 diabetes.
- Early insulin initiation in Type 2 diabetes with an early focus on postprandial rise in glucose is important.
- Pen devices have made it easier for people with diabetes and are preferred over the syringe and vial; however, there is a need for a higher maximum dose, a low-dose injection force and an ability to differentiate devices injecting different insulins, which were not met by pens already on the market.
- The novel SoloSTAR® pen addresses these needs with a larger maximum dose (80 units) and a lower injection force, and is available in distinct body colors, with tactile features on the dose knob to differentiate between the insulin glargine and insulin glulisine pens. Dose accuracy testing demonstrated that SoloSTAR pens are very accurate and consistently deliver the dialed doses of insulin.
- Studies have demonstrated that the SoloSTAR pen is easy to teach and easy to learn, which may save healthcare professional time, is easy to use with a low-dose injection force and is preferred by more patients than the FlexPen® and Lilly pen®.
- The SoloSTAR pen is therefore suitable for a wide range of patients with Type 2 diabetes, particularly those taking both basal and prandial insulin, and for patients with visual or dexterity disorders.

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