Smart Connected Insulin Pens, Caps, and Attachments: A Review of the Future of Diabetes Technology

Nikhil A. Sangave,[1] Timothy D. Aungst,[2] and Dhiren K. Patel[1]

The evolution of technologies to manage diabetes has led to improvements in patient adherence, technique, and monitoring. Insulin pens, for example, have distinct advantages over vials and syringes; they allow for more accurate dosing, improved adherence, less injection site pain, and greater patient satisfaction (1,2). As the population with diabetes grows internationally, second-generation insulin pens have been engineered with USB or Bluetooth features to enable closer monitoring of pharmacotherapy. Similarly, many devices for self-monitoring of blood glucose have also become integrated with Bluetooth to enable wireless transmission of data to a smartphone.

As of 2016, the smart insulin pen market was valued at $59 million and is expected to increase to $123 million by 2023 in Latin America, the Middle East, and Africa (3). One report predicts that Europe will have the greatest smart insulin pen market growth, bringing in more than $2 million by 2027, based in part on high current utilization of such pen devices. The trend toward increased use of smart insulin pens can also be seen in North America; in fact, the same report estimates that, by 2027, the North American smart insulin pen market will have a continuous annual growth rate of 26.7% (4).

The emergence of new technologies such as smart insulin pens, caps, attachments, and virtual platforms can help both patients and health care providers (HCPs) overcome problems such as poor insulin adherence, incorrect insulin initiation and titration, and medication errors. Adoption of such new devices may increase even further if clinical trials can show long-term cost-effectiveness (5).

This review highlights the technologies now available on the market in the United States and internationally that are designed to improve insulin administration. A comprehensive literature review was conducted using manufacturer websites, press releases, commercial data resources, educational and training tools, news outlets, periodicals, and medical device databases. Clinical trial information was included where possible, but limited studies have been conducted in this field to date. This review only includes devices that can be used as standalone products.

Digital Health Advancements for Insulin Pens

The widespread adoption of the Internet of Things (integration of wireless connectivity sensors into devices and objects) and the proliferation of digital health tools has led to a phase of mass development of new tools in medical care. Taking the commonly used insulin pen and adding sensors or technological features to update it for care in the 21st century has become a small niche, with multiple companies creating their own platforms or devices. The two most pervasive models at present are pens with refillable insulin cartridges that

[1]MCPHS University, Boston, MA

[2]MCPHS University, Worcester, MA

Corresponding author: Dhiren K. Patel, dhiren.patel1@mcphs.edu

https://doi.org/10.2337/ds18-0069

feature built-in wireless communication abilities and sensors to track insulin delivery. Other companies are creating sensors that attach to disposable insulin pens, such as a cap or a device that attaches to the side of the pen. These two approaches are targeted to currently produced insulin pens (i.e., pens with refillable cartridges or disposable pens) and reflect geographic regional preferences for insulin pen utilization. The following sections describe these devices in more detail.

Integrated Smart Pen Systems

The features of available integrated smart pen systems are summarized in Tables 1 and 2.

In December 2017, Companion Medical had a limited launch of its InPen system. The product includes a reusable pen that is compatible with U-100 (3 mL) lispro (Humalog, Eli Lilly) and aspart (Novolog, Novo Nordisk) rapid-acting insulin cartridges. The system is available by prescription only through a mail-order pharmacy.

After the insulin cartridge is appropriately installed, the device sends real-time data via Bluetooth to an InPen application (app) available for iPhones. The app displays information such as whether the pen is exposed to temperature extremes. Users can record their most recent blood glucose levels and anticipated meals, and a dose calculator will recommend the correct amount of insulin to inject. Of note, InPen can make the distinction between insulin used to prime the device and insulin for administration. Once the insulin is injected, the amount injected is also recorded on the app. Each pen has a non-rechargeable battery that lasts ~1 year (6,7) (Table 1).

In 2007, Eli Lilly made an early investment in the digital health market when it released the HumaPen Memoir in Europe. At the time, the pen featured a digital display and memory of the dates and times of the most recent 16 insulin doses. The product was lauded for its ability to minimize insulin waste and for accurate dosing but was ultimately discontinued for commercial reasons (8,9).

More recently, Eli Lilly announced in December 2017 that it would start feasibility studies to create a connected ecosystem of diabetes management using its automated insulin delivery (AID) system (10). With this system, the company is aiming to bring a hybrid closed-loop platform (using an insulin pump, a continuous glucose monitoring [CGM] device, and a dosing algorithm) to the market that can help patients dose their insulin based on real-time CGM. In addition, another platform includes the use of a "connected insulin pen with glucose-sensing technologies and software applications" to give patients insulin dose recommendations (10). Currently, Eli Lilly has received U.S. Food and Drug Administration (FDA) 510K clearance for a dosing app called the Go Dose System that can supply insulin dosing information for patients using Eli Lilly insulin products (11). Two versions of the app will be available, "Go Dose" for patients and "Go Dose Pro" for HCPs, enabling providers to titrate patients' insulin doses remotely. Further details regarding these new pen-related devices are not yet available.

Novo Nordisk has also started investing in and conducting clinical trials of decision-support systems to help minimize hypoglycemia in patients with type 1 diabetes (12). One of its newest pen models is called the NovoPen 5. These pens are compatible with U-100 (3 mL) aspart rapid-acting insulin cartridges and can administer 1- to 60-unit single doses. The pen clicks once a full dose has been administered. Its electronic display shows the last dose of insulin administered. It also has the capacity to display the hours elapsed since the last injection, the pen battery life, and information on malfunctioning pen memory (Table 2).

The NovoPen Echo is a similar pen device created for children. It offers the same features as the NovoPen 5, but allows for half-unit dosing and only administers up to 30 units of insulin per injection (13) (Table 2).

Novo Nordisk recently announced plans to release its NovoPen 6 and NovoPen Echo Plus in 2019. These products will eventually replace and improve on the designs of the NovoPen 5 and NovoPen Echo (14).

The German company Pendiq Intelligent Diabetes Care has created Pendiq 2.0 digital insulin pens. To date, these devices are only available in Germany. Pendiq 2.0 pens are compatible with U-100 (3 mL) lispro and aspart rapid-acting insulin cartridges. They are able to store the last 1,000 entries of injection dates, times, and quantities, and users can view these entries on an OLED display. The pen's Bluetooth compatibility allows it to transmit the data to a proprietary smartphone app called dialife, which is available for both Android and Apple smartphones. The pen comes with a USB cable used to both transmit data to a computer and recharge the pen battery. The device features a motor-driven apparatus that allows more precise dosing in increments of 0.1 units. Pendiq 2.0 also has a safety alarm that notifies users of any low insulin levels, low battery power, or malfunctions (15) (Table 1).

The ESYSTA system is another device in the smart connected insulin pen arena and is a product of Emperra Digital Diabetes Care. ESYSTA pens are compatible with U-100 (3-mL) lispro, aspart, and glulisine (Apidra, Sanofi) rapid-acting insulin cartridges. The device stores 1,000 entries, and its batteries must be replaced yearly. The display shows the last dose of insulin administered and a countdown during the actual insulin injection. The ESYSTA pen can wirelessly transfer insulin doses, times, and dates to the ESYSTA app, which is available for both Android and iPhone smartphones. The app provides users with blood glucose

TABLE 1. Overview of InPen, ESYSTA, Pendiq, and YpsoMate SmartPilot Smart Insulin Pens

	InPen	ESYSTA	Pendiq	YpsoMate SmartPilot
Company	Companion Medical	Emperra	Pendiq	YpsoMed
Country of origin	United States	Germany	Germany	Switzerland
FDA approval	2016	No	No	No
U.S. availability	Yes	No	No	No
Cost	$665	$220 (€192)*	$193 (€169)*	Unable to verify
Insulin compatibilities	Lispro/aspart 3-mL cartridges	Lispro/aspart/glulisine 3-mL cartridges	Lispro/aspart 3-mL cartridges	Prefilled insulin
App service	Apple, Android	Apple, Android	Apple, Android	Unable to verify
Bluetooth	Yes	Yes	Yes	Yes
USB	No	No	Yes	No
Features	• Lasts 1 year • Temperature sensor • Dose calculator • Reminders for patient • Prescription needed	• Cloud database accessible to providers • Replaceable batteries (last for up to 1 year) • Memory capacity for 1,000 data records	• Memory for recording last 1,000 injections (date, time, quantity) • Alarms if low battery, needle blockage, or low insulin • Rechargeable battery	• Tracks injection time and sequence of handling (pressing against skin, triggering the injection, positioning the injector, end of injection)

**Currency conversions conducted on 29 January 2019.*

TABLE 2. Overview of NovoPen 5 Plus, NovoPen Echo, Vigipen, and KiCoPen Smart Insulin Pens

	NovoPen 5 Plus	NovoPen Echo	Vigipen	KiCoPen
Company	Novo Nordisk	Novo Nordisk	Diabnext	Cambridge Consultants
Country of origin	United States	United States	United States	United Kingdom
FDA approval	No	Yes	No	No
U.S. availability	No	Yes	No	No
Cost	$68 (~£52)*	~$54–$67 with discount	Unable to verify	Unable to verify
Insulin compatibilities	Aspart 3-mL cartridges	Aspart 3-mL cartridges	Unable to verify	Unable to verify
App service	No	No	Apple	Unable to verify
Bluetooth	No	No	Yes	Unable to verify
USB	No	No	No	Unable to verify
Features	• Records time since and dose of last injection • Displays battery life and memory status	• Designed for children • Records time since and dose of last injection • Displays battery life and memory status • Half-unit dosing	• Automatically records the time of injection as well as the amount of insulin injected • Transfers the data via Bluetooth to app	• Records time and amount injected

**Currency conversions conducted on 29 January 2019.*

trends and targets and the ability to synchronize their data to the ESYSTA Portal, a real-time interface that users and their HCPs can use to track insulin administration and blood glucose levels. The data are encrypted and protected in compliance with the International Organization for Standardization and the International Electrotechnical Commission (16) (Table 1).

Cambridge Consultants, based in the United Kingdom, has pioneered the KiCoPen, which recently received the prestigious, international Red Dot Award for product design. The pen connects wirelessly to a smartphone app, which tracks the times and amounts of insulin injected and allows users to input glucose levels, exercise regimens, and carbohydrate consumption. The device derives its power not from battery storage, but rather from the kinetic energy of the cap being pulled off of the pen (17) (Table 2).

Smart Sensors and Attachments for Insulin Pens

YpsoMed's YpsoMate SmartPilot is a reusable attachment to the proprietary YpsoMate pen, designed for an easy two-step injection process. The device has a sensor and memory that connects with an app to display injection timing and doses. The sleeve is intended for a single use and is disposal. The emphasis with this product is on injection process; the pen can provide audio and visual feedback to users. The app can also remind users when it is time to inject. When data are shared with an HCP, adherence and injection technique can be assessed—specifically any errors in the handling or administering of the insulin (18) (Table 1).

The features of available smart caps and insulin pen attachments are summarized in Tables 3 and 4.

The GoCap, by Common Sensing, is a device that replaces the caps of Solostar (Sanofi), KwikPen (Eli Lilly), and FlexPen (Novo Nordisk) insulin pens. The Joslin Diabetes Center is conducting a clinical trial in which the app platform and GoCap devices are provided to a sample of patients using these pens. The primary outcome measure is missed insulin doses (19).

The GoCap app is available for both iPhone and Android users. The cap itself uses light sensors to detect how much insulin remains and has a screen that shows the quantity of insulin in the pen once a dose has been administered and the pen properly recapped. It also shows that the insulin has been administered successfully by displaying a check mark on the screen. The cap can be recharged with the provided micro-USB cable, and its battery lasts for 10 days.

The cap needs to be paired via Bluetooth to the mobile app. The app not only displays the type and time of insulin administration, but also allows users to enter blood glucose levels and meals. Alerts let users know when their next injection should be and whether there are any temperature fluctuations. The information provided can be shared by entering an e-mail address on the app (20) (Table 3).

Timesulin, by Bigfoot Biomedical, is a cap that records the time since the last injection. When the cap has been removed from the pen for 8 seconds, it resets. When the cap is put back on the pen, it begins timing again. The caps are compatible with KwikPen, FlexPen, FlexTouch (Novo Nordisk), and SoloStar insulin delivery devices. The product is meant to minimize extra or missed doses of insulin and can be used for ~1 year (21) (Table 3).

Dukada Trio is a cap with novel features that place an emphasis on proper injection technique. The cap is compatible with FlexPen and SoloStar devices. Dukada, a company based in Denmark, has designed the cap to have a flexible grip feature that, when extended, allows for more stability for patients with dexterity problems. The cap also features a light above the needle to improve visibility when injecting. The cap has small lights that illuminate every hour after insulin administration to remind the user when the last dose was injected. According to Dukada, the cap has a replaceable battery that lasts for 6–8 months (22) (Table 3).

InsulCloud, based in Spain, created a product called InsulClock. This is an attachment currently used with the KwikPen, although the company plans to make it available for several major insulin pens, including the Flextouch, Flexpen, and SoloStar. Unlike the caps, this attachment snaps on to the back of the insulin pen and logs how much insulin is administered on an app available for both iPhone and Android smartphones. Similar to the other apps and devices, the platform shows the type, time, and quantity of insulin administered and can provide users with reminders. The app also reports any temperature fluctuations and allows users to store their food or blood glucose data (23) (Table 4).

Diabnext has made a similar product called Clipsulin. The device is compatible with the majority of pen devices on the market, including the SoloStar, ClikSTAR (Sanofi), KwikPen, Luxura (Eli Lilly), FlexPen, and FlexTouch brands. Clipsulin records the amount of insulin injected. As the user turns the knob to adjust the insulin dose, the device detects the units of insulin being queued for injection, and its LED display shows that number. Once injected, the quantity is transmitted to the app via Bluetooth. Clipsulin uses the Diabnext app available for both iPhone and Android smartphones. Similar to the other platforms, the app allows for long-term blood glucose trending, diet logging, and medication reminders. According to Diabnext, the device's battery lasts for ~1,800 injections and the device can hold 200 injections in memory (24). (Table 4).

InsulCheck, by the Irish company Innovation Zed Ltd., is a similar attachment that records time elapsed between injections. The green light on the attachment displays after the user

TABLE 3. Overview of Smart Caps

	GoCap	Timesulin	Dukada Trio
Company	Common Sensing	Bigfoot Biomedical	Dukada
Country of origin	United States	United Kingdom	Denmark
Year created	2013	2010	2012
FDA approval	No	No	No
U.S. availability	Yes	No	No
Cost	$25/month	$15.72 (~£12)*	$46 (~ €40)*
Insulin compatibilities	SoloStar pens, FlexPen, and KwikPen (2019) pens	KwikPen, FlexPen, FlexTouch, SoloStar pens	FlexPen, SoloStar pens
App service	Apple, Android	No	No
Bluetooth	Yes	Yes	No
USB	Yes	No	No
Features	• Displays remaining insulin • App displays type/time of insulin administration • App allows for blood glucose monitoring and meal entry • Lasts 1 year	• Tracks the time since last injection • Battery life of 1 year	• Flexible grip allows for more stability • Has a light above needle for better visibility • Shows time elapsed since last injection

**Currency conversions conducted on 29 January 2019.*

TABLE 4. Overview of Insulin Pen Attachments

	InsulClock	Clipsulin	EasyLog	InsulCheck
Company	InsulCloud	Diabnext	BioCorp	Innovation Zed, Ltd.
Country of origin	Spain	United States	France	Ireland
FDA approval	No	No	No	No
U.S. availability	No	No	No	No
Cost	$285 (€249)*	~$40	<$50	~$32
Insulin compatibilities	KwikPen, FlexTouch, SoloStar pens	SoloStar pens, ClikSTAR, KwikPen, Luxura, FlexPen, FlexTouch	Unable to verify	FlexPen, KwikPen, SoloStar pens, NovoPen 3/4/5/Echo, Luxura HD, Savvio, ClikSTAR
App service	Apple, Android	Apple, Android	Unable to verify	No
Bluetooth	Yes	Yes	Yes	No
USB	No	No	No	No
Features	• Shows the type, time, and quantity of insulin administered • App provides dose reminders, food/glucose input, temperature fluctuations	• Shows the type, time, and quantity of insulin administered • Battery life of 1,800 injections • Memory of 200 injections	• Detects time, date, amount of insulin injected • Alerts patients about missed, extra, and next doses	• Records elapsed time between injections • Green light flashes when dose injected • Temperature sensor • Replaceable battery

**Currency conversions conducted on 29 January 2019.*

delivers a dose and the time resets. The attachment is compatible with a wide array of pens, including FlexPen, SoloStar, KwikPen, NovoPen 3/4/5/ Echo, Luxura HD, Savvio (Eli Lilly), and ClikSTAR. InsulCheck has a small replaceable battery and alerts users if their insulin has been exposed to temperature fluctuations (25) (Table 4).

BioCorp, a French company, is releasing a similar product called EasyLog. This device has two attachments—one for the dosage knob and one on the handle encasing the dose window. The device detects the time, date, and amount of each insulin injection. These data are then transferred to a proprietary app. EasyLog can also alert users if double doses have been administered, doses have been missed, or it is time to take the next dose. BioCorp says the device is compatible with all major pens but does not specify each product (26) (Table 4).

Discussion

This brief article illustrates a changing dynamic in the integration of digital health technologies in the insulin pen market. Whereas many startup companies have sought to create sensors that attach to insulin pens or other devices that work with insulin cartridges for patient dosing and management, the past few years have seen a shift within the pharmaceutical sphere. Currently, insulin manufacturers, including but not limited to Eli Lilly, Sanofi, and Novo Nordisk, appear to be expanding their interest in this area and creating their own systems and products that may either integrate with current companies in this arena (based on previous investments) or become direct competitors with fully integrated smart insulin pen devices. Ultimately, costs and payor coverage will likely determine which companies will emerge as the main players in the digital health sphere for diabetes management.

In summary, the development of new pens, caps, and attachments for insulin delivery holds great promise for improving diabetes management. These devices may offer the potential for improved adherence, administration, and quality of care. Smart devices have even been tailored to other conditions such as asthma and hypertension, showing that the landscape for chronic disease management is significantly adapting to new technologies. Smart connected pens, devices, and attachments may aid in minimizing the long-term costs and complications of diabetes and improve diabetes care overall.

Duality of Interest

D.K.P. has been a consultant to and serves on advisory boards and speakers bureaus for Novo Nordisk and Sanofi. No other potential conflicts of interest relevant to this article were reported.

Author Contributions

N.A.S., T.D.A., and D.K.P. all equally researched, wrote, and edited the manuscript. All three authors are the guarantors of this work and, as such, had full access to all of the research and take responsibility for the integrity and accuracy of the information presented.

References

1. Pearson, T. Practical aspects of insulin pen devices. J Diabetes Sci Technol 2010;4:522–531

2. Bariya M, Nayberg I. Analysis of "Dose accuracy, injection force, and usability assessment of a new half-unit, prefilled insulin pen." J Diabetes Sci Technol 2017;12:373–375

3. Wood L. LAMEA smart insulin pens market 2017–2023: ResearchAndMarkets.com. 23 March 2018. Available from www.businesswire.com/news/home/20180323005439/en/LAMEA-Smart-Insulin-Pens-Market-2017-2023--. Accessed 25 July 2018

4. Saha S. Smart insulin pens market to grow at a CAGR of 17.9% through 2027: future market insights. 16 July 2018. Available from globenewswire.com/news-release/2018/07/16/1537595/0/en/Smart-Insulin-Pens-Market-to-Grow-at-a-CAGR-of-17-9-through-2027-Future-Market-Insights.html. Accessed 25 July 2018

5. Klonoff DC, Kerr D. Smart pens will improve insulin therapy. J Diabetes Sci Technol 2018;12:551–553

6. Gildon BW. InPen smart insulin pen system: product review and user experience. Diabetes Spectr 2018;31:354–358

7. Companion Medical. InPen. Available from www.companionmedical.com/InPen. Accessed 15 June 2018

8. Ignaut DA, Venekamp WJ. HumaPen Memoir: a novel insulin-injecting pen with a dose-memory feature. Exp Rev Med Devices 2014;4:793–802

9. Beschizza R. Huma-Pen Memoir insulin injection system. Wired June 2017. Available from www.wired.com/2007/02/humapen-memoir-. Accessed 12 December 2018

10. Eli Lilly. Lilly initiates clinical trial to evaluate the functionality and safety of its automated insulin delivery system. December 2017. Available from lilly.mediaroom.com/index.php?s=9042&item=137733. Accessed 12 December 2018

11. Kiang T. U.S. Food and Drug Administration letter of approval of the Go Dose System. December 2016. Available from www.accessdata.fda.gov/cdrh_docs/pdf16/K160949.pdf. Accessed 7 April 2019

12. ClinicalTrials.gov. Efficacy of inControl Advice: a decision support system (DSS) for diabetes. Available from clinicaltrials.gov/ct2/show/NCT03093636?term=novo+nordisk+insulin+pen&draw=2&rank=14. Accessed 12 December 2018

13. Novo Nordisk. Introducing NovoPen 5. Available from www.novonordisk.com/patients/diabetes-care/pens--needles-and-injection-support/NovoPen5.html. Accessed 15 June 2018

14. Novo Nordisk. Novo Nordisk plans first global launch of connected insulin pens and announces key digital health partnerships. Available from www.globenewswire.com/news-release/2018/10/01/1600412/0/en/Novo-Nordisk-plans-first-global-launch-of-connected-insulin-pens-and-announces-key-digital-health-partnerships.html. Accessed 5 October 2018

15. Pendiq. Pendiq 2.0. Available from pendiq.com/en/insulin-pen. Accessed 15 June 2018

16. Emperra. ESYSTA pen. Available from www.emperra.com/en/esysta-product-system/pen. Accessed 15 June 2018

17. Cambridge Consultants. Red Dot Design Award for KiCoPen. Available from www.cambridgeconsultants.com/press-releases/red-dot-design-award-kicopen. Accessed 15 June 2018

18. YpsoMed. SmartPilot for YpsoMate: reusable add-on transforms YpsoMate into a fully connected device. Available from yds.ypsomed.com/en/injection-systems/smart-devices/smartpilot.html. Accessed 15 June 2018

19. ClinicalTrials.gov. Insulin dosing practices in persons with diabetes on multiple daily injections. Available from clinicaltrials.gov/ct2/show/record/ NCT02914730?term=insulin+pen+smartphone&rank=2. Accessed 12 December 2018

20. GoCap. How it works. Available from gocap.me/how-it-works. Accessed 21 June 2018

21. GoldLife. A timer for the insulin pens you already use: Timesulin. Available from timesulin.com. Accessed 21 June 2018

22. Dukada. Diabetes management with DUKADA Trio for your insulin pen. Available from www.dukada.com/features-diabetes-management/#grip. Accessed 21 June 2018

23. InsulClock. Be part of the revolution. Evolve in your diabetes. Available from www2.insulclock.com/en. Accessed 29 June 2018

24. Diabnext. Clipsulin C3: make your pen smart. Available from www.diabnext.com/insulin-clipsulin. Accessed 29 June 2018

25. InsulCheck. Diabetes isn't a choice. How you manage it is. Available from www.insulcheck.com/products. Accessed 29 June 2018

26. BioCorp. BIOCORP receives CE mark approval for its smart cap Easylog. Available from biocorpsys.com/wp-content/uploads/2018/10/PR_BIOCORP_Easylog.pdf. Accessed 29 June 2018