

scPharmaceuticals



SENSILE MEDICAL

LARGE-VOLUME INJECTOR ENABLES ANYTIME ANYWHERE DELIVERY OF PARENTERAL DRUGS

In this piece, Pieter Muntendam, MD, President and CEO, scPharmaceuticals; Gerhard Mayer, PhD, Vice-President, Business Development North America, Sensile Medical USA; and Lars Krinelke, MD, PhD, Head Product Management, Head Medical Affairs, Sensile Medical AG describe how their large-volume injection device allows subcutaneous self-administration, an important part of the “anytime-anywhere” model for drug delivery.

Many important drugs must be administered parenterally because they are not orally active or are insufficiently orally active to remedy a specific condition. With rare exceptions, parenteral administration requires intravenous (IV) or intramuscular (IM) administration by a specially trained clinician. To date, subcutaneous (SC) administration has not been an option for many pharmaceuticals despite the conceptual appeal of a simpler, less invasive drug delivery option. scPharmaceuticals aims to change that – using innovative technology to enable anytime-anywhere treatment options that benefit patients, clinicians, healthcare facilities and payers.

SC administration is appealing in several ways. It provides nearly 100% bioavailability, in most cases offers a preferred pharmacokinetic profile over the standard IV bolus, and does not require special skills. From a patient’s perspective it is also less invasive than IV administration. However, its use for parenteral drugs has been restricted by technology. SC delivery by injection is limited to 1-1.5 ml. Larger volumes of a drug would require a slower rate of administration that is not possible with a syringe and needle. Except for insulin and treatments for certain orphan disorders, none of the commonly used parenteral medications have been developed for slow SC administration.

scPharmaceuticals was formed to develop new SC treatments based on existing and widely used parenteral drugs. The first such therapy will be a novel formulation of the

loop diuretic, furosemide, for heart failure.

Novel technology allows for simple, convenient and comfortable SC administration of parenteral pharmaceuticals in larger volumes than has been possible before. scPharmaceuticals partnered with Sensile Medical to develop an easy-to-use, full-featured patch pump device that permits SC drug administration over durations, rates and volumes that can be tailored to specific drugs.

PART OF THE ANYTIME-ANYWHERE MEDICAL MODEL

SC administration of parenteral drugs, and eventually self-administration of those drugs, is an important part of the emerging anytime-anywhere medical model that seeks to align medical treatments and processes more closely with the fluidity of daily life. Technology enables patients to communicate with clinical staff in real time. Clinical data and even results of blood tests can be transmitted allowing the physician to make informed clinical decisions.

We are at the dawn of a new medical model where time and place are almost irrelevant. In this model physicians can authorise use of more advanced therapies and patients can self-administer medications that previously required visits to a medical facility or home visits from a healthcare professional. SC self-administration of critical medications as envisioned by scPharmaceuticals is a natural component of this new model.



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In the emerging model there are two distinct clinical scenarios or use cases where SC administration offers clear and obvious benefits:

1. Supplementing IV with SC

SC administration offers effective parenteral therapy that bridges current treatments. The use of furosemide in heart failure provides an illustration. Oral furosemide at home and intravenous furosemide in the emergency room or hospital are currently essential in heart failure treatment. SC furosemide for use at home offers an intermediate treatment to prevent the exacerbation of symptoms that now require emergency room or in-hospital treatment, and avert the need for IV treatment. SC furosemide can also be used to continue treatment at home following a patient's discharge so as to extend parenteral treatment without the need to prolong the in-patient stay. In this case SC treatment is not used to replace IV, but to supplement existing options and give patients the kind of therapeutic response that was previously available only in an emergency room or hospital.

2. Substituting SC for IV

Many parenteral antibiotics are administered IV. Instead of daily administration of an antibiotic in a peripherally inserted central line (PIC line or PICC), a patient could receive SC treatment using a patch pump whilst continuing to go about normal daily living. Thus, instead of driving to an infusion centre, for example, the patient can drive to work while the small patch pump on the abdominal wall conveniently and comfortably provides the same dose of the same drug. The benefits are distinct and important – avoidance of the cost and complications of the PIC line, and avoidance of the cost and personal burden of the administration in an infusion centre or doctor's office.

UNTAPPED OPPORTUNITY WITH LARGE POTENTIAL

The safety of most widely used parenteral medications is well established but their use has been restricted to a clinical setting because intravenous or intramuscular administration requires clinical skills and has inherent risks. SC administration of parenteral drugs has simply not been an option with existing technologies, making the benefits of convenient comfortable anytime-anywhere administration of parenteral prescription pharmaceuticals unobtainable.



Figure 1: The heart of SenseCore Technology: Sensile's micropump consisting of two plastic components.

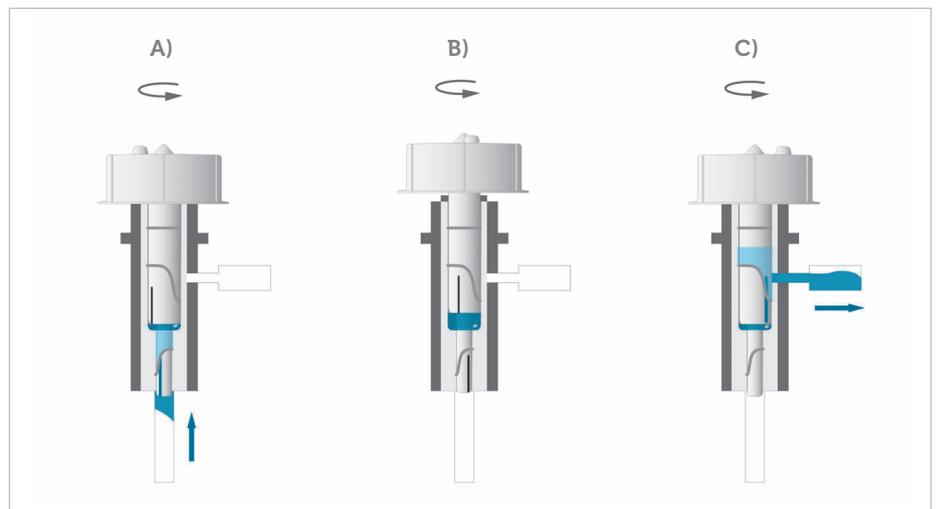


Figure 2: A) As the pump rotates, the upward motion draws in the exact dose. B) The dose resides in the pump with both valves closed, preventing uncontrolled free-flow. C) With continued rotation and the downward stroke, the drug is expelled toward the needle and the patient.

Determined to overcome the technology barrier, scPharmaceuticals explored a range of technologies and options for large volume injectors. After evaluating all available options, scPharmaceuticals selected Sensile Medical's SenseCore technology for its wearable patch pump. SenseCore is a micro piston pump, smaller than the size of a US "quarter" coin, comprising two pieces of precision moulded medical grade plastics (see Figure 1). The piston is rotated by a small electric motor and the rotation provides the pumping force (see Figure 2). The pumping can be bi-directional allowing the device both to fill itself from a standard primary container and to deliver the medication SC.

Until now devices used a single component design wherein the mechanism that provided the force and energy was part of the component that delivered the drug, thus the entire device had to be discarded after use. In most designs this also meant

the device had to contain a filled medication reservoir using non-standard primary containers and closures. These devices were complex, expensive and difficult to manufacture, and thus not suitable for routine widespread use.

The SenseCore technology allows for the development of a small two-component device comprising a single-use disposable unit and a reusable unit (see Figure 3). The disposable unit contains the SenseCore pump, a drug reservoir, the fluid path, needle insertion and retraction mechanism, and the patch that adheres to the skin during drug delivery. The reusable unit consists of a motor, controller and electronics in plastic housing. After inserting the disposable cartridge in the reusable unit, a mechanical drive shaft connects the two to transfer the energy and force.

As mentioned previously, Sensile's technology is being developed to deliver scPharmaceuticals' furosemide heart failure



Figure 3: The Sensile pump is a customised delivery device. In this configuration, it consists of two major parts. In the disposable part, a micropump draws the product out of the reservoir and delivers it through a needle on the underside of the device (not shown). Key high-value components are retained for repeated use in the reusable part. During administration, only the disposable part is in contact with the drug or the patient. After injection, only the disposable is discarded.

treatment. Figure 3 shows an overview of the disposable and reusable components of the furosemide delivery system. In Figure 4, the disposable and reusable components are combined and the drug vial has been attached for automatic transfer of the drug into the internal reservoir. Finally, in Figure 5, the vial has been removed and the furosemide patch is ready for use.



Figure 4: The patient transfers the drug from the vial into the device's internal reservoir. Upon completion of transfer, the vial is removed.

In general, the SenseCore technology offers a number of important benefits:

- **Auto-fill from standard primary container:**

The device for scFurosemide has an auto-fill feature that allows it to fill itself from a standard primary container such as a vial. This eliminated the need to design a new primary container and closure system, and avoided the associated development and regulatory risks. Additionally, it eliminates the need bring the device into the pharmaceutical manufacturing process. The drug and device have separate manufacturing processes and come together in a much simpler kitting process.

- **Controlled Delivery of Large Volume:**

Furosemide and other therapies in the pipeline will require administration of larger volumes than possible with syringes and needles – up to 20 ml. The electromotor and controller allow full control over the delivery. The device has a dynamic range that spans a range from 50 µl over 24 hours to 5 ml per minute. The electromotor and controller permit every possible required delivery profile, including one that provides multiple distinct administrations – for example it is possible to administer four doses of 5 ml at six-hour intervals. In this case the

device can be filled with multiple doses that, if administered IV, would require multiple resource-intensive drug administrations by a clinician.

- **Platform for Multiple Applications:**

This design includes capability to auto-fill from a standard container and delivery controlled by a pre-programmed computer chip. These features permit a single device to be used across a broad range of therapies by changing only the software programming that controls the fill and delivery.

- **Optimising Pharmacokinetics:**

For some drugs, such as antibiotics, maintaining plasma levels is critical to achieving therapeutic effects. For other drugs, a rapid loading dose is desirable followed by a steady-state delivery. The electronic control allows for optimisation of delivery to achieve the desired therapeutic effects. In many cases the controlled delivery with the patch pump can offer an improved pharmacodynamic response when compared with the same dose administered by the standard once-a-day IV bolus.

- **Cost Efficiency:**

Many of the clinical situations where conversion from IV to SC offers important advantages require frequent drug administration over extended periods. For example, antibiotics usually require daily doses for weeks or even months. This puts pressure on the cost of goods associated with the components that are discarded after each administration. With a two-component design, the reusable component can be used for the entire treatment period and only a low-cost, single-use component is discarded after each drug administration.

- **Advanced Proprietary Features:**

One important feature of the SenseCore technology is the built-in opportunity to monitor its pumping function. As the micro piston pump operates, the piston will make short up-and-down movements with every rotation in the housing. The piston's up-and-down movements can easily be monitored using an electronic sensor in the reusable unit. This enables important safety features typically not possible with other technologies. In case of blockage of the fluid path, for example, the sensor would register impaired piston movement which could trigger a “malfunction” alarm. These features would be complex and expensive to match with most other technologies

since they would require fluid path sensors. Another important feature is that needle insertion and retraction are electronically controlled and do not use a mechanical spring for release. The advanced features of the system are patent protected.

scPHARMACEUTICALS' PIPELINE

The company's lead product is scFurosemide - a novel formulation of furosemide injection optimised for SC delivery. The Affordable Care Act provides unprecedented financial incentives for hospitals to improve management of patients with heart failure and reduce readmission rates following patient discharge. scFurosemide allows physicians to increase diuresis in heart failure patients and reduce fluid overload to prevent the acute form of heart failure known as acute decompensated heart failure. It can also be used to finish a treatment regimen at home that was started in the hospital. The patient would be discharged after a short stay in a medical facility and continue SC furosemide at home for 3-5 days until fluid overload has been resolved.

A second product that scPharmaceuticals plans to bring to market will be the first ever cephalosporin antibiotic for SC administration. This will offer convenient and comfortable administration, and eventually self-administration, that will replace the need for a PIC line, and daily trips to an infusion centre or clinic for intravenous administration. Similarly, it will avoid the costs and complications associated with PIC lines for outpatient parenteral antimicrobial treatment in the home-setting.

scPharmaceuticals expects to file US NDAs for both products in 2015 and to launch the products in 2016.

MEETING HEALTHCARE PROVIDER AND PATIENT NEEDS

Human factor considerations are playing an ever-increasing role, especially as novel drug delivery systems are coming to market. Professionals, patients and caregivers may need to be able to safely prepare, place, activate and remove the device with minimal difficulty. The SenseCore technology allows for single-button operation with visual and audible signals that are easy to understand. The devices are pre-programmed at the time of manufacturing for the drug delivery profile. This eliminates the risk of programming errors by user or clinician.



Figure 5: Now ready for use, the device is placed on the skin and the drug administered. After injection, disposable and reusable parts are separated and only the disposable is discarded.

TIME TO CLINIC OR MARKET

The option to use a standard primary container, combined with the auto fill feature, eliminates the need for development and testing of a novel primary container and a separate fill facility for the container. This can reduce time to clinical use or market by several years, as new primary packaging alone will typically take 4-5 years. It also removes an important component and risk to the regulatory review.

TRAIL-BLAZING ON A PATH TO THE MARKET

A patch pump straddles the domains between auto-injectors and infusion pumps. It acts as an advanced large form of auto-injector with controls and safety features that are typically absent from auto-injectors. However, structurally it resembles an infusion pump. In the case of the Sensile system it contains a mechanical pump driven by an electromotor controlled by a circuit board. Infusion pumps are subject to increased scrutiny by the regulatory agencies in response to errors and malfunctions that have caused injury or death. Pre-programmed delivery using a patch pump that is easy to use should avoid the problems associated with the programmable pumps.

As is often the case, release of a first-of-its-kind product for use will define a path making it easier for others to follow. The SenseCore technology is well suited to blaze the trail and set the standard because of its combination of precision, controls and advanced safety features.

ABOUT scPHARMACEUTICALS INC

scPharmaceuticals was formed in 2013 to develop innovative pharmaceutical products for SC delivery based on widely-used and proven APIs. scPharmaceuticals is pursuing the largely untapped opportunity of treating patients for serious and life-threatening conditions with convenient anytime-anywhere SC drug administration. scPharmaceuticals is developing a portfolio of innovative drug-device combination products that use the SenseCore micro piston technology for delivery. This technology allows for a cost-effective two-component design. For further information see www.scpharmaceuticals.com.

ABOUT SENSILE MEDICAL AG

Sensile Medical AG is a leading company in the area of advanced micro pump technology developing a broad range of customer-specific delivery and dosing solutions. These pumps are increasingly being used to enable for instance Large-Volume SC delivery of modern pharmaceutical and biotech products for self-administration by patients. Due to Sensile's SenseCore technology the products are highly cost-efficient, accurate, and safe. They are increasingly used in drug delivery, medical and consumer applications. Founded in 2004, Sensile Medical is located in Haegendorf, Switzerland. For further information consult: www.sensile-medical.com.

Sensile Medical is the ideal partner for individualised drug delivery solutions



Applications for the SenseCore Technology

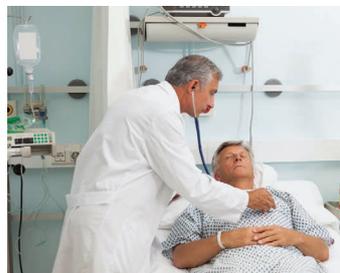
Patch pump
for up to 20 ml drug delivery

Key benefits

- Highly accurate volumetric dosing from simple to complex flow rates
- Primary container independent solution
- Automated needle insertion and retraction mechanism
- Sophisticated, but simple sensor technology
- Well-known rotary piston pump technology with proven production capabilities
- Economical reusable – disposable designs with all fluid-contact items in the disposable



Home care



Hospital care



Diagnostics



Drug preparation



SENSILE
MEDICAL

SMART
SIMPLE
SUSTAINABLE

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