SteadyMed
THERAPEUTICS

PATCHPUMP: EXPANDING THE LIMITS OF PARENTERAL ADMINISTRATION

Here, Marylyn Rigby, Director of Business Development & Marketing, SteadyMed Therapeutics, introduces the company's PatchPump device, its design, mechanism of action, steps of use and current status of clinical development.

SteadyMed Therapeutics is a specialty pharmaceutical company redefining the parenteral delivery experience and is committed to expanding the limits of injectable therapeutics to restore freedom, joy, and dignity to patients' lives. The company is actively developing a portfolio of PatchPump™-enabled drug products and intends to submit its first US NDA in the second half of 2015, as further described below.

INTRODUCTION TO PATCHPUMP™

PatchPump is a proprietary system developed by SteadyMed, to enable easier, more convenient and less error-prone drug administration via a single-use, disposable, prefilled (at the site of manufacture under aseptic conditions), pre-programmed drug-device combination product.

PatchPump is highly customisable, and is intended to deliver volumes up to 10 ml, over a period of minutes or a number of days depending on the delivery needs of the particular therapy and disease state.

The core technology inside the PatchPump is the E-Cell, which is comparable to an alkaline battery but with a flexible housing. The key difference between the E-Cell and a conventional alkaline battery is that as the E-Cell discharges, the housing expands. In the PatchPump, the expansion of the E-Cell is precisely controlled by its electrical discharge rate, and as the E-Cell expands against a flexible drug reservoir, the liquid formulation is expelled from the device and delivered either subcutaneously or intravenously.

The PatchPump utilises either an external infusion set as used with insulin infusion pumps (see Figure 1), or an integrated cannula (see Figure 2) to deliver the medication.

In addition to the E-Cell, the other major components of the PatchPump include: a flexible container for the prefilled sterile drug formulation; a programmable circuit board, containing the hardware and software that control the discharge/expansion rate and other device functions; various sensors to assist in flow control and occlusion detec-

Figure 1: PatchPump configured for external subcutaneous infusion set.

Figure 2: The PatchPump together with integrated cannula.

Marylyn Rigby
Director of Business Development & Marketing
T: +1 925-272-4999
E: mrigby@steadymed.com

SteadyMed Therapeutics, Inc
2410 Camino Ramon, Suite 285
San Ramon
CA 94583
United States

www.steadymed.com

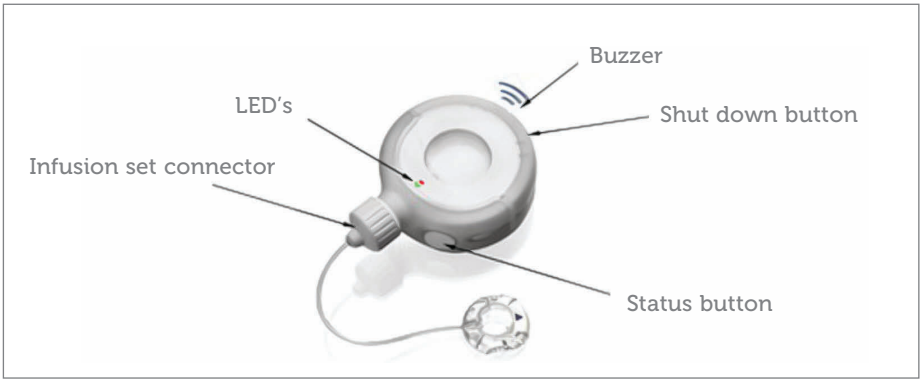


Figure 3: The PatchPump incorporates a number of sensors, and indicators that provide feedback to the patient. (Infusion set configuration shown here.)

tion, and other indicators to tell the patient the status of the drug delivery (Figure 3).

In the configuration developed for SteadyMed's lead internal development programme; treprostinil PatchPump for pulmonary arterial hypertension (PAH), the PatchPump will utilise an external infusion set, and will be programmed to deliver drug continuously for a number of days. At the end of the dosing period, PatchPump will alert the patient that it is out of drug; the patient removes and disposes of the empty device, and replaces it with a new unit to continue the chronic, around-the-clock infusion treatment.

This multi day replacement frequency is consistent with, or better than; the interval currently used for refilling other pumps used for PAH infusion therapy. Further, in contrast to the existing parenteral therapies for this indication, the use of SteadyMed's PatchPump-enabled product will eliminate the need for users to handle or fill the pump with drug, as well as the need for any dose programming.

Future PatchPump configurations for other products may run for shorter or longer periods, and may have the same existing external infusion set or may have an integrated infusion set.

PRINCIPLE OF OPERATION

To activate the treprostinil PatchPump PAH product, the user removes a cap from the discharge port and attaches an infusion set at that location. This action pierces the septum of the primary drug container and simultaneously turns on the product. (For the integrated PatchPump configuration, which may be used to deliver biologic compounds, pressing a small button, which inserts the soft cannula into the subcutaneous tissue, activates the device.) Once activated, the E-Cell begins to expand at a controlled rate and as it does it displaces the piston, which applies positive pressure to the drug container. The pressure on the container forces drug solution through the delivery channel of the container and into the infusion line at a controlled rate.

The rate of expansion of the E-Cell is related to its discharge current. The movement of the piston is measured using standard sensor technology, and a control circuit in the electronics ensures that the piston moves at the required rate by regulating the discharge current (and hence the rate of expansion) of the E-Cell. If there are any occlusions in the delivery line, or site of infusion, they are detected by a force sensor positioned on the printed circuit board (PCB) underneath the E-Cell (Figure 4). The increase in force produced by an occlusion is sensed by the control system, which triggers an alarm and stops the E-Cell expansion.

During basal delivery the product is silent unless the status button is pressed, in which case the buzzer sounds and the LEDs flash green. Near the end of the delivery period the product will beep and LEDs will be illuminated to instruct the user that delivery will soon end.

It is expected that the PatchPump will usually be positioned on the patient's abdomen but sites may also include the upper arm, hip, thigh and upper buttocks. The product is intended to be self-administered, and it is intended to be applied, used and worn throughout the course of normal daily activities. Hence the product may experience the environments associated with working, exercising, sleeping and be worn both indoors and outdoors. In addition, PatchPump is designed to be water resistant and can be worn while bathing or swimming.

E-CELL™

The E-Cell is a patented electrochemical actuation unit invented and developed by SteadyMed. The materials of construction of the E-Cell are comparable with a standard alkaline battery cell , with the exception that the cell materials are contained in a flexible polymer housing to allow for expansion. Figure 5, a schematic of the E-Cell, shows the anode and cathode materials contained in a flexible housing that also contains the electrolyte solution. When the product is activated, current is allowed to flow via the electrical connectors to resistors in the control circuit on the PCB. This causes the electrochemical reaction inside the E-Cell to take place, which results in a change in volume of the anode and cathode materials. The geometric design of the anode and cathode along with the flexible housing ensure linear, unidirectional expansion of the E-Cell (in the vertical direction as oriented in Figure 5). The quantities of anode and cathode material ensure that the E-Cell has sufficient capacity to support expansion throughout the entire infusion cycle for the product.

Given the E-Cell acts as its own power source and the driving motor that effects drug delivery the PatchPump can deliver viscous drugs and large volumes from a small compact form factor.

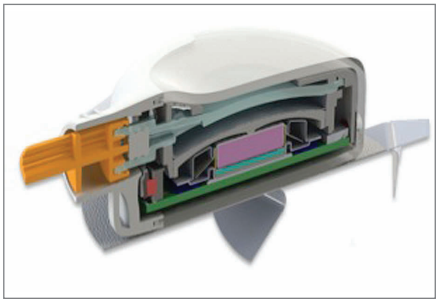


Figure 4: Cross-sectional view showing the components layered within the PatchPump.

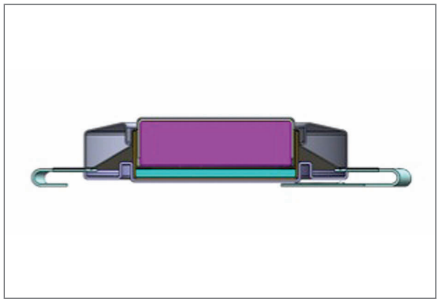


Figure 5: Schematic cross-section of the E-Cell.

Figure 6: The primary drug container comprises a flexible multi-laminate blister heat-sealed to a rigid base plate, with integrated filling/discharge channel, sealed with a butyl rubber septum.

PRIMARY DRUG CONTAINER

The primary drug container is circular in design and made up of several components. A flexible, thermoformed multi-laminate blister is heat-sealed to a rigid, injection-moulded base plate with an integrated filling/discharge channel. The blister and base-plate materials have been used in prior pharmaceutical and medical device applications, and were selected because of their low levels of extractables, and compatibility with biologic drugs. The container is sealed with a butyl rubber septum. An additional cap is fitted during the aseptic filling process, to maintain the cleanliness of the exterior surface of the septum, up to the point of use of the product.

The container has been tested for drug compatibility, long-term stability and leachable compounds, and results have all been favourable. Additional studies by third party biopharmaceutical companies have been conducted for compatibility with biologic compounds, with favorable results for adsorption and leachables as well as drug stability.

CLINICAL AND HUMAN FACTOR STUDIES.

As a part of PatchPump development a series of Human Factors (HF) studies have been completed with physicians, specialist healthcare practitioners (HCPs), patients and healthy volunteers. This empirical work has been informed and supported by an iterative program of design risk assessment activities, including risk reviews of existing devices and Use FMEA studies.

The series of HF studies has provided a foundation of understanding of the users (patients and HCPs), and their current experiences in order to inform device design features and parameters to support safe and effective use. Several URS and PRS requirements were derived from these studies as well as a deeper understanding of users' acceptance and subjective preferences around the key principles of the drug device combination concept. In addition these studies provided the direction to help develop the PatchPump and Instructions for Use (IFU) design and provided good insight into the potential patient interaction with the design. This series of studies led to further refinement of the user interface and IFU.

SteadyMed has conducted proof-of-concept clinical studies in healthy volunteers in order to evaluate the safety, tolerability and technical aspects of the PatchPump. Data from these studies is undisclosed.

DEVELOPMENT STATUS

SteadyMed's PatchPump is in late-stage development with the supply chain in place to manufacture registration batches of its treprostinil PatchPump product prior to NDA submission in the second half of 2015.

The company is also working with biopharmaceutical companies that are assessing stability and compatibility of certain biologic drugs with the PatchPump as well as the performance of market research studies.

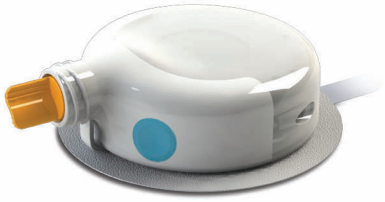
(PRE)FILLED WITH CONFIDENCE

PatchPump by SteadyMed Therapeutics, Inc.

SteadyMed is about to expand the delivery limits of parenteral therapeutics with PatchPump® the world's leading pre-filled and pre-programmed liquid drug delivery platform that's not only customizable but discreet.

Learn how to get pre-filled with the confidence that will transform how parenteral therapies are delivered.

Learn more at **SteadyMed.com**



Watch us transform.