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YPSODOSE: SIMPLIFYING LARGE-VOLUME PATCH INJECTION FOR PHARMA COMPANIES AND PATIENTS

In this article, Ian Thompson, Vice-President Business Development, Delivery Systems, Ypsomed, provides an update on YpsoDose, a new prefilled large-volume patch injector platform, and how it is designed to simplify the approach to wearable patch injectors for both pharma companies and patients.

MARKET REQUIREMENTS FOR PATCH INJECTORS

There are many large-volume injectable drugs, mainly antibody (mAb)-based, in pharmaceutical development for the treatment of diseases such as rheumatoid arthritis, psoriasis, IBD/Crohn's, asthma, dermatitis, cardiovascular disease and migraine. Looking into the future, the demand for them will be further increased by immuno-oncology drugs as maintenance therapies for treated cancers.

General expectations for these drugs are that they will be dosed subcutaneously every two weeks, monthly or even less frequently; that the dosage will be in the 3–10 mL range; and that the injection will require 5–30 minutes.[1] The large injection volume and longer injection time compared with autoinjectors mean that the injection system needs to be worn on the skin during administration. A skin worn patch injector requires a new drug reservoir compared with a prefilled syringe-based autoinjector, which is held against the skin for around 10–20 seconds.

> "Developing and designing a wearable patch injector is demanding and requires a broad range of technology and medical device know-how."

The possible selection of a wearable patch injector continues to compete against more frequent dosing regimes using standard prefilled syringe-based autoinjector therapies. If pharma companies want to consider and invest in patch injectors, they need to be able to access reliable device technology, utilise standard filling processes and, last but not least, fully understand patient preferences. Fulfilling these requirements will allow the patch injector market to grow significantly over the coming years and establish itself as a third self-injection device class to complement the well developed markets for pens and autoinjectors.

LARGE-VOLUME SUBCUTANEOUS INJECTION CHARACTERISTICS

Biologics and mAb-based therapeutics have a large therapeutic window and allow the use of a large fixed-dose drug payload, making them compatible with a patch injector. The overall dose and protein concentration may be quite high, impacting drug stability and viscosity, drug processing and injection forces. For example, the protein concentration of blockbuster biologic drugs, such as adalimumab and trastuzumab, is in the 50–150 mg/mL range and total payloads for a single dose may be as high as 600 mg or greater. Additionally, a positive development trend is the general move from other routes of administration, such as intravenous (IV)

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infusions to subcutaneous administration, in order to reduce the higher proximal and physical administration costs.[2]

Whatever the type of subcutaneous therapy, there are a number of established therapies confirming that the overall injection flow rates for such drugs are best suited to the 0.33–1.00 mL/minute range. Examples include:

- Immunoglobulins that are injected in the 20–30 mL/h range
- 3 mL dose of evolocumab that is injected over nine minutes
- 5 mL dose of trastuzumab (containing hyaluronidase) that is injected at approximately 1 mL/minute.

YPSODOSE PATCH INJECTOR OVERVIEW

Developing and designing a wearable patch injector is a demanding task that requires a broad range of technology and medical device know-how. Ideally, the less frequently used patch injector should be as easy to use as a disposable two-step autoinjector, therefore the 3–10 mL prefilled YpsoDose format (Figure 1) incorporates the following key technical features:

- Prefilled and fully disposable to remove any need to assemble the drug reservoir and device, thus eliminating potential handling errors by the patient.
- Adheres well to the skin during injection, is easy to remove after injection and the sensing patch only allows initiation of the injection after contact with the skin, to eliminate an accidental or premature start of injection.
- YpsoDose automatically inserts the injection needle at the start and retracts the needle at the end of the injection process. The needle is also retracted if YpsoDose is removed from the skin before the end of injection.
- A stepper-motor drive, which accommodates a range of fill volumes and viscosities, drives the injection, providing a reproducible injection time for each drug.
- The onboard electronics incorporate wireless connectivity and provide audible and visual signals to clearly communicate with the patient before, during and after the injection.

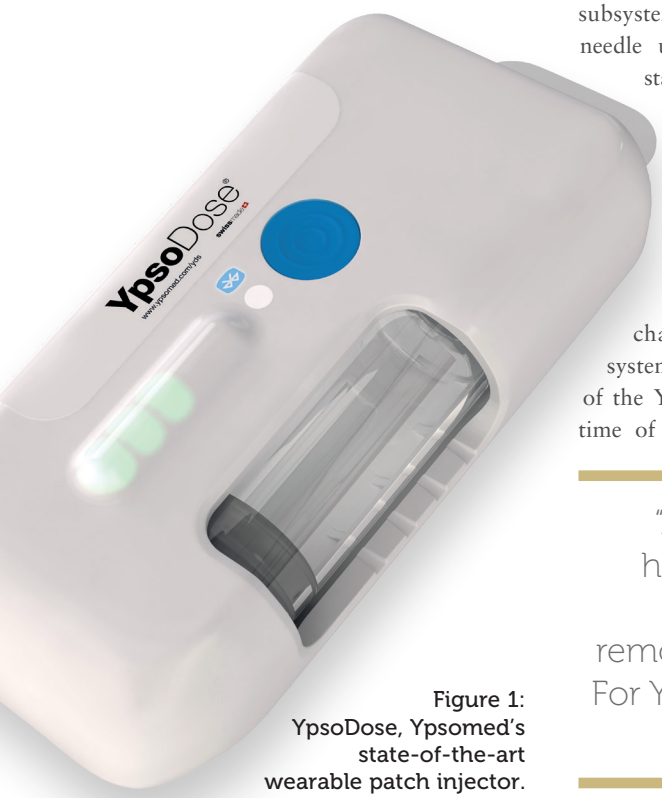

Figure 1: YpsoDose, Ypsomed's state-of-the-art wearable patch injector.

SIMPLIFYING DRUG FILLING AND FINAL ASSEMBLY

These wearable patch injector features and aspects are covered by YpsoDose's electromechanical systems. However, one key aspect is the ability to prefill the device and maintain the sterility of the drug reservoir and fluid path during its lifetime. YpsoDose achieves this by incorporating a bespoke sterile fluid path enclosed within an encapsulated, sterile subsystem, called the needle unit. The needle unit can be compared with the staked needle and rigid needle shield of a prefilled syringe. Whereas the drug in the prefilled syringe is directly connected to the fluid path, within the YpsoDose needle unit the fluid path is completed only on injection.

The cartridge, being a well characterised container closure system, does not interact with the rest of the YpsoDose injector until the actual time of injection. The interface between the cartridge and needle unit has been designed to allow the cartridge to be filled on conventional filling equipment, either in bulk or ready-to-fill tub formats. Ypsomed is continuing to work closely with pharma partners, cartridge component manufacturers and filling equipment and contract filling specialists to ensure that standard components and filling processes can be utilised.

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> "Ultimately, if patch injector therapies are going to be adopted widely for biologic therapies, usability is the most important aspect that needs to be successfully tested with patients."

YPSODOSE USABILITY UPDATE

Ultimately, if patch injector therapies are going to be adopted widely for biologic therapies, usability is the most important aspect that needs to be successfully tested with patients. Current systems are generally healthcare provider (HCP) or patient filled or assembled; no prefilled, ready-to-use wearable devices are currently approved for use by patients. Human factors work with YpsoDose is ongoing to prove and optimise the patch system and user interface. The skin sensor system is key to ensure that the injection can only be initiated once YpsoDose is correctly attached to the skin, as well as to minimise the number of steps required to perform the injection (Figure 2).

All in all, the YpsoDose handling steps are like a two-step autoinjector: remove the cap and inject. For YpsoDose this is simply patch and inject. All other steps

Figure 2: YpsoDose worn on the body.

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are controlled by YpsoDose, guiding the patient when to push the injection button and providing feedback throughout the injection process. At the end of injection the needle is retracted and YpsoDose is ready for disposal or specialist recycling.

The most recent human factor studies in the US, performed with the first generation 5 mL YpsoDose format across a wide range of different user groups, have confirmed that:

1. All participants completed successful injections on the first attempt.
2. The user interface is simple and easy to understand, with the orientation of the device proving intuitive when placing it on the body.
3. Participants were comfortable with YpsoDose's size and weight, especially with the understanding that it is a single-dose, infrequent injection.
4. Participants were generally comfortable and not worried when wearing the device. The injector did not prevent them from completing daily activities.
5. The look and feel of the device were acceptable because participants would generally administer this injection in the comfort of their home.

Based on the feedback from the latest studies, the functional prototype design has been finalised for use in pharma customer feasibility studies. As shown in Table 1, based on the comfort rating scale[3] scores, participants rated the most critical dimensions of YpsoDose's wearability the lowest (i.e. Harm, Emotion and Anxiety) confirming that the participants do not negatively score these dimensions. The overall CRS score of 4.3 means that participants generally felt that YpsoDose was comfortable to wear for the duration of the injection.

In summary, Ypsomed is committed to the successful development and commercialisation of YpsoDose as a new state-of-the-art wearable patch injector. Achieving this requires Ypsomed to drive collaboration with key partners, including pharmaceutical companies and drug reservoir and filling specialists, in addition to needing to understand patient characteristics and needs completely.

Dimension	Statements	Mean
Emotion	I am worried about how I look when I wear this device. I feel tense and on edge because I am wearing the device.	2
Attachment	I can feel the device on my body. I can feel the device moving.	9
Harm	The device is causing me some harm. The device is painful to wear.	1
Perceived change	Wearing the device makes me physically different. I feel strange when wearing the device.	5
Movement	The device affects the way I move. The device inhibits or restricts my movement.	6
Anxiety	I do not feel secure wearing the device.	3

Table 1: YpsoDose's wearability rating as a summary of comfort rating scale results. Participants (N=17, adult, adolescent and elderly patients) rated their level of agreement with the following statements from 0 (Disagree) to 20 (Agree).

ABOUT THE COMPANY

Ypsomed is the leading independent developer and manufacturer of innovative self-injection and insulin pump systems for self-administration. Within the Delivery Systems business unit the customisable product platforms cover autoinjectors for prefilled syringes in 1 mL and 2.25 mL format, disposable pens for 3 mL and 1.5 mL cartridges, reusable pens and easy-to-use injection devices for lyophilised drugs in dual-chamber cartridges. Unique click-on needles and infusion sets complete the broad self-injection systems product portfolio. The 3–10 mL YpsoDose patch injector draws on Ypsomed's depth of expertise in diabetes care with fully connected insulin pump systems. Ypsomed provides its partners with excellent technological expertise and full regulatory support for the device relevant aspects of the registration process.

The injection systems are developed and manufactured in Switzerland with strong in-house competencies covering concept and product development, tool-making, injection moulding and automated assembly. Ypsomed is ISO 13485 certified and all processes are run according to design control and cGMP guidelines with operational QA/QC experts on-site at each location. Ypsomed's US FDA-registered manufacturing facilities are regularly inspected by both pharma customers and regulatory agencies and supply devices for global markets including the US, Europe, Japan, China and India. Ypsomed has more than 30 years' experience and well-established working relationships with numerous leading pharma and biotech companies.

REFERENCES

1. *Mathaes R et al, "Subcutaneous Injection Volume of Biopharmaceuticals-Pushing the Boundaries". J Pharm Sci, Aug 2016, Vol 105(8), pp 2255–2259.*
2. *Tetteh EK, Morris S, "Evaluating the administration costs of biologic drugs: development of a cost algorithm". Health Econ Rev, Dec 2014, Vol 4(1), p 26.*
3. *Knight JF, Baber C, "A tool to assess the comfort of wearable computers". Hum Factors, 2005, Vol 47(1), pp 77–91.*

ABOUT THE AUTHOR

Ian Thompson has been with Ypsomed AG, formerly Disetronic AG, since 1995 in a number of roles in key account management and business development working with pharma companies to develop and bring to market innovative self-injection systems. He studied biochemistry and biotechnology in the UK and has worked in medical device companies since moving to Switzerland in 1990. Since 2003 his main focus has been business development and new product innovation leading to the successful development and launch of a range of new pen and autoinjector custom products for Ypsomed Delivery Systems.

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- Unique electromechanical drive system for a range of viscosities and fill volumes

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