

# YPSOMED

## SELFCARE SOLUTIONS

# REDUCING THE COMPLEXITY OF LARGE-VOLUME SELF-INJECTION FOR PHARMA COMPANIES & PATIENTS

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

### MARKET REQUIREMENTS FOR WEARABLE INJECTORS

Larger-volume injectable drugs are in pharmaceutical development and being considered for the treatment of auto-immune diseases such as rheumatoid arthritis, psoriasis and IBD/Crohn's disease. Looking into the future their demand will be further increased by new drugs for treating diseases like migraine, asthma and dermatitis, and immuno-oncology drugs as maintenance therapies for treated cancers.

General expectations for these drugs is that they will be dosed subcutaneously every two weeks, monthly or even less frequently; that they will be in the range 2-10 mL; and that the injection will require 5-15 minutes.<sup>1</sup> The longer time of injection compared with auto-injectors means that injection systems need to be worn on the skin during administration. And, a skin-worn wearable injector requires a different drug reservoir compared with an auto-injector. The need to maintain a flexible sterile fluid path and needle system between the drug reservoir and the skin means that a cartridge is the drug container of choice. Cartridges have known container closure integrity characteristics and utilise existing filling processes and infrastructure.

Wearable injector therapies will ultimately be competing against more frequent dosing based on standard prefilled syringe-based therapies. For pharma companies to consider and invest in wearable 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 wearable injector market to grow significantly over the coming years and establish itself as a third self-injection device class to complement the already well developed markets for pens and auto-injectors.

### VOLUMES & VISCOSITIES: IMPACT ON THE WEARABLE INJECTOR

Biologics and antibody-based therapeutics have a large therapeutic window and allow the use of a fixed dose payload. This means, though, that often the overall dose and thus protein concentration is quite high, which influences drug stability and viscosity, drug processing and device injection forces.

The typical protein concentration of blockbuster biologic drugs is in the 50-150 mg/mL range and total payloads for a single dose may be high as 600 mg or greater. Examples of biotherapeutics with their concentrations and dose volumes are provided in Table 1.

There is also significant experience for therapies that require large payloads for systemic release such as the use of immunoglobulins for the treatment of immunodeficiency, and here up to 50 mL of antibody is infused using re-usable pumps and multiple infusion sets. Also, there is a general move to subcutaneous (SC) administration in order to reduce the higher proximal and



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Drug	Indication	Pharma Company	Dose / Volume	Concentration (mg/mL)
Adalimumab	Autoimmune diseases	AbbVie	40 mg / 0.4 mL	100
Etanercept	Autoimmune diseases	Amgen / Pfizer	50 mg / 1 mL	50
Trastuzumab	Oncology	Roche	600 mg / 5 mL	120
Evolocumab	Hyperlipidaemia	Amgen	420 mg / 3 mL	140

**Table 1: Examples of biologic drugs, with their doses and concentrations.**

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physical administration costs associated with other routes of administration such as intravenous infusions.<sup>2</sup>

Our recent interactions with big pharma companies active in the auto-immune and oncology therapeutic areas confirm that the 2-10 mL SC injection is the most likely volume range for wearable injectors. Whatever the type of SC therapy, there are a number of references confirming the overall injection flow rates are in the 0.33-1.00 mL/min range. Examples include: immunoglobulins that are injected in the 20-30 mL/hr range or 1 mL / 2-3 min; 3 mL of evolocumab is injected in 9 min; and 5 mL of trastuzumab containing hyaluronidase is injected at approximately 1 mL/min.

Being able to accommodate different flowrates and viscosities within a wearable injector platform requires a reliable and flexible drive mechanism. This is why YpsoDose (see Figure 1) incorporates a standard electromechanical drive that provides the necessary forces capable of achieving the maximum flowrates of 1 mL/min at high protein concentrations.

### WEARABLE INJECTOR NEEDS

Developing and designing a wearable patch injector is demanding and requires a broad range of technology and medical

device know-how. Ideally, the wearable injector, which is used less frequently, should be as easy to use as a disposable two-step auto-injector, which means it needs to incorporate the following key technical features:

- Prefilled and fully disposable to remove any need to assemble the drug reservoir and device
- Easily adhere to the skin during injection; and be easy to remove after injection
- Automatically insert the injection needle at the start and retract or shield the needle at the end of the injection process.

In order to be truly versatile and easy to use, the device also needs to be able to deal with the following aspects:

- Cover a range of fill volumes and viscosities and provide a reproducible injection time per drug
- Recognise that the device is only ready to inject when attached to the skin
- Communicate clearly with the patient via advanced audio and visual signals before, during and after the injection
- Offer wireless connectivity for additional services.

### REDUCING COMPLEXITY FOR PHARMA WITH A READY-TO-FILL FORMAT

The wearable patch injector features and aspects just listed are covered by YpsoDose's electromechanical systems. But particularly important is the ability to prefill the drug reservoir and incorporate the sterile unit into the device in a simple and robust way.

Being prefilled and fully disposable, and to remove any need for the patient to assemble the drug reservoir, the device requires a bespoke fluid path which, in the case of YpsoDose, is provided by the Needle Unit. The Needle Unit can be

compared with the staked needle and rigid needle shield of a prefilled syringe. But, 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 Needle Unit and cartridge are pre-assembled in a terminally sterilised tub format (Figure 2, next page) to provide an intrinsically stable ready-to-fill unit which is compatible with existing filling equipment.

Ypsomed is working closely with cartridge component manufacturers, filling equipment and contract filling specialists to make sure that generally available and standardised cartridge components are utilised in this bespoke ready-to-fill format. The cartridge, being a well characterised container closure system, does not interact with the rest of the injector until the actual time of injection.

### USABILITY ASPECTS: PATIENT INTERFACE, 2-STEP WEARABLE, PATCH AND INJECT

Ultimately, if wearable injector therapies are going to be adopted widely for biological therapies, usability is the most important aspect that needs to be successfully tested with patients. Current systems are generally filled or assembled by the healthcare



**Figure 1: The YpsoDose prefilled large-volume patch injector platform.**

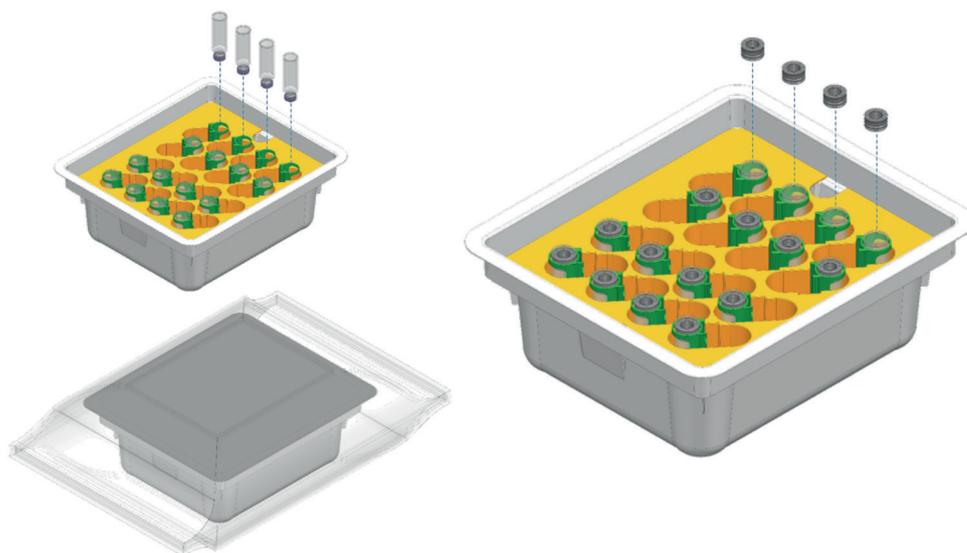


Figure 2: Cartridge and Needle Unit in the ready-to-fill tub format. Left: Cartridge-Needle Unit assembly prior to EtO sterilisation. Right: Cartridge filling in ready-to-fill format.

“All-in-all the YpsoDose handling steps are like a two-step auto-injector: remove the cap and inject. For YpsoDose this is simply: patch and inject. All other steps are controlled by YpsoDose.”

professional or patient. 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, and to minimise the number of steps required to perform the injection.

All-in-all the YpsoDose handling steps are like a two-step auto-injector: remove the cap and inject. For YpsoDose this is simply: patch and inject. All other steps 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 made safe and YpsoDose is ready for disposal or specialist recycling.

In summary, Ypsomed is committed to the successful development and commercialisation of YpsoDose as a new state-of-the-art wearable patch injector. This requires Ypsomed to drive collaboration

with pharmaceutical companies, and drug reservoir and filling specialists in addition to completely understand patient characteristics and needs.

#### ABOUT THE COMPANY

Ypsomed is the leading independent developer and manufacturer of innovative auto-injector and pen injector systems for self-administration. The customisable product platforms cover auto-injectors for prefilled syringes in 1 mL and 2.25 mL format, disposable pens for 3 mL and 1.5 mL cartridges, re-usable pens that include automated injection mechanisms and easy-to-use injection devices for drugs in dual-chamber cartridges such as lyophilised drugs. Unique click-on needles and infusion sets complement the broad self-injection systems product portfolio. Ypsomed provides its partners with excellent technological expertise and full regulatory support for the device relevant aspects of the registration process.

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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 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

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#### 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 from 1979 to 1983, working initially in commercial roles for fermentation technology. He 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 auto-injector Custom Products for Ypsomed Delivery Systems.

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For more information visit [www.ypsomed.com/yds](http://www.ypsomed.com/yds)

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