



DELIVERING VALUE FOR INJECTABLES: UNMET NEEDS, DEVICE SOLUTIONS & THERAPEUTIC OUTCOMES

What constitutes value today for an injectable drug or vaccine? That's a question increasingly being asked by patients, prescribers and payers when it comes to the selection and use of injectable therapies. While upfront price will always be important, there are multiple other factors now being used by healthcare stakeholders to determine how a particular brand of injectable therapy should be valued against its competition. This article, from Stephen Allan, Senior Vice-President, Strategic Planning, Unilife Corporation, examines why pharmaceutical companies are leveraging innovative delivery systems to enhance and differentiate their injectable products so that they can generate powerful value-based healthcare outcomes amongst payers, prescribers and patients.

GENERATING VALUE-BASED HEALTHCARE OUTCOMES VIA SAFER, SIMPLER, SMARTER DEVICES

Patients, prescribers and payers all have a key role to play in determining what brand of therapy will be used in the treatment of chronic diseases. Each of these stakeholder groups are motivated by a different set of factors that together can determine their brand of preference. For a pharmaceutical company seeking to optimise the use of its product against brand-name or biogeneric competitors to build or protect market share, it is important to pursue a multifaceted strategy that distinctly resonates across each of these audiences.

Promoting the distinctive molecular characteristics of a therapy alone is insufficient in this regard. In addition to demonstrating the pharmacokinetics and pharmacodynamics of an injectable molecule, pharmaceutical companies today must also showcase how it can enhance patient care, maximise therapy compliance and minimise healthcare costs. To maximise rates of preference and acceptability, a more holistic approach is required to showcase the value of the entire therapeutic package. In short, the value proposition for a therapy must extend beyond the drug itself to focus instead on the drug-device combination product.



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PATIENTS

Patients are becoming increasingly brand-aware regarding their therapy options, and highly influential in the selection of which brand they are prescribed. When it comes to selecting one competing brand of therapy against another, drug delivery systems are becoming a central factor in the decision making process.

Safety, simplicity and convenience of use are all of paramount importance from a patient perspective. How does the therapy fit within a patient's normal daily routine? Does it minimise the frequency of injection? Does it minimise the pain and discomfort associated with each injection? Is it so safe and simple to use that it minimises the risk of dosing error or drug wastage? Is it compact in size and ergonomic to hold? Can it be readily used in any environment such as the home, office, café or gym? Can it provide automatic reminders to the patient's smart phone on when the next dose is due, or preferred injection settings?

The capacity of a drug delivery device to address factors such as these fully can be critical in driving rates of patient preference and acceptability for a particular brand of injectable therapy, and enhance the likelihood of a pharmaceutical company building a long-term relationship with the patient.

PAYERS

Payers are vigorously encouraging the shift to the patient self-injection of injectable therapies to reduce healthcare costs and improve patient quality of life. However, a high rate of patient non-adherence across many chronic disease areas represents a significant financial drain on the healthcare systems.

To improve healthcare productivity and maximise rates of therapy adherence, many payers recognise that there are two core priorities in the supply and administration of injectable therapies for patient self-administration.

First, injectable therapies must be made as safe, simple and convenient as possible for patients to adhere to their medication regimes. As the primary interface between drug and patient, the ergonomic design, features and functionality of a drug delivery system are integral to the provision of patient-centric therapies that minimise common medication challenges including incorrect or missed doses. For categories such as wearable injectors, devices are even helping to enable or accelerate the treatment of chronic diseases outside of healthcare facilities.

Second, payers are seeking to gain better insight into how patients are utilising their prescribed therapies outside of healthcare facilities. In particular, the integration of Bluetooth LE within drug delivery systems such as auto injectors and wearable injectors represents a significant opportunity to leverage the power of data informatics. With access to real-time and historic data regarding compliance to a therapy regime, payers and prescribers will be better positioned to determine which particular therapy brand can deliver the most favourable long-term return on investment, regardless of upfront cost. Where multiple brand-name or biogeneric

able to provide therapies in a device format that addresses these prescriber preferences will be in a strong position to build or protect market share against competitors with inferior data-driven outcomes.

CREATING VALUE FOR PHARMACEUTICAL CUSTOMERS

To better serve the needs of patients, payers and prescribers, and generate powerful brand differentiation for their injectable therapies against the competition, pharmaceutical companies are shifting rapidly to the use of innovative drug delivery

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options are available, the value of this data may be instrumental in determining what level of market share a pharmaceutical company captures within the relevant therapy area.

PRESCRIBERS

Data informatics also represents a significant opportunity to bridge the gap between patients and prescribers. As one example, the prescription of an insulin pump with integrated Bluetooth connectivity to an insulin-dependent patient with Type 2 diabetes would allow an endocrinologist to tailor a therapy regime better, to help reach the patient's HbA1c goals. As another example, a prescriber with accurate, reliable access to a patient's specific history of injections will enable them correlate whether a recent adverse healthcare episode was caused by non-adherence or dosing error.

As prescribers are forced to manage an increasing number of patients within only a finite period of time, they will become even more attracted to the productivity gains and patient care enhancements attainable through the prescription of therapies leveraging smarter, simpler and more convenient devices. Pharmaceutical companies who are

systems to contain and administer injectable therapies. However, with each target therapeutic segment or drug indication having specific unmet or emerging needs, a one-size-fits-all approach to drug delivery systems is not feasible.

While each therapy segment and patient population has unique requirements, Unilife has experienced market success by pursuing a platform-based strategy whereby each device it develops must adhere to the following criteria:

- It must address significant unmet market needs
- It must be straightforward to industrialise by the pharmaceutical customer, and able to fit into standard drug filling and packaging systems
- It must minimise regulatory risk by utilising standard materials within the primary drug container
- It must be so safe, simple and convenient to use that it adds real value for patients, prescribers and payers
- It must be highly differentiated from the competition, and user-preferred; and
- It must be able to be sold at a price that represents real value for the pharmaceutical customer.



Figure 1: EZMix Prodigy™ platform – dual-chamber single-barrel prefilled syringes.

To demonstrate the flexibility of how this approach can be leveraged by pharmaceutical companies to enable, enhance and differentiate their injectable drugs across a range of therapy areas, this article provides examples of unmet needs and available device solutions for immuno-oncology, diabetes, vaccines and auto-immune diseases.

ADDING VALUE IN IMMUNO-ONCOLOGY

Therapeutic products to treat oncology have traditionally required IV infusion, with patients having to visit specialty care clinics or other healthcare facilities to receive treatment over several hours. For healthcare providers, the administration of such products is a complicated, time-intensive process with multiple pieces of equipment required to reconstitute and administer the dose. Patients receiving treatment also face a significant social and financial burden, with frequent facility visits, significant discomfort and high out-of-pocket costs. Payers are also acutely conscious of the high costs associated with IV infusion, including not only the purchase of the drug, but various ancillary pieces of equipment.

To support pharmaceutical companies seeking to address such unmet needs for oncology and immuno-oncology, Unilife has created a range of innovative platform tech-

nologies that can reduce cost and complexity, and potentially accelerate a shift in the place of treatment from the clinic to the home.

For drugs that require reconstitution and / or IV infusion, Unilife has created the EZMix Prodigy™ platform of dual-chamber single-barrel prefilled syringes (Figure 1). EZMix Prodigy products enable the automatic, ventless and orientation-free reconstitution or mixing of liquid-liquid combination products or lyophilised drugs up to 50 mL in volume with one simple step. The products can also be configured for universal connectivity with IV ports or needleless luer access devices.

Where a pharmaceutical company has an approved or pipeline immuno-oncology therapy, such as a monoclonal antibody, that is being targeted for subcutaneous administration, Unilife also has multiple delivery platforms available that can facilitate its simple and convenient administration by patients outside of healthcare facilities. In addition to prefilled syringes and smart-reusable auto injectors (see below), Unilife has developed a market-leading portfolio of wearable injectors to accommodate drugs requiring either dose volumes between 1 mL and 15 mL, or extended delivery periods over minutes or hours (Figure 2a and 2b). Prefilled, pre-assembled and supplied ready to administer a measured dose of drug at a preset rate and duration, Unilife's wearable injectors require only three steps to commence the initiation of therapy, and are equipped with an array of customisable features including Bluetooth LE connectivity.

ADDING VALUE IN INSULIN PUMPS

The current generation of insulin pumps has not been widely embraced within the Type 2 market, and only partially within the Type 1 market, due to device complexity, reimbursement constraints and high out-of-pocket cost for patients.

Upfront costs for durable insulin pumps can range up to US\$7,000 (£4,530). There are

then additional significant ongoing monthly costs for infusion sets and other peripherals. Disposable patch pump systems can be more expensive on a monthly basis. Such high upfront and monthly costs make insulin pumps less attractive for use within the Type 2 market. Insulin pumps are also bulky, and require intensive training before use. Multiple pieces of equipment are required, many of which require a separate prescription. Numerous steps are needed to begin insulin infusion therapy, with many more required to facilitate bolus delivery at mealtimes.

Unilife recognises that to gain broad acceptance across insulin-dependent people with diabetes, a patch pump technology must have minimal steps to commence basal therapy, as well as simple on-demand bolus delivery. It must be a fully integrated, prefilled insulin therapy solution that is so compact, convenient and discreet that it empowers patients to live a normal life by reducing the daily burden of diabetes treatment. Furthermore, it must minimise upfront and ongoing monthly costs for continuous insulin infusion therapy, so that it becomes as attractive for reimbursement as prefilled disposable insulin pens. And finally, just like insulin pens, it must leverage the established sales and distribution channels of diabetes market leaders.

Unilife has addressed these market requirements with the creation of Imperium™, the world's first platform of instant patch pumps for insulin (Figure 2c).

Imperium requires far fewer steps to commence therapy than any other known durable pump or insulin patch pump. A key reason for this competitive advantage is that it can be prefilled and pre-assembled with insulin. Just like with insulin pens, insulin providers can supply their brand of therapy in one fully integrated system ready for immediate patient use and covered under just one prescription. Unlike with all other known insulin pumps, there is no need for patients to load the device with insulin before use. Furthermore, patients do not



Figure 2: Unilife's platform of wearable injection devices: (a) The Precision-Therapy™; (b) The Flex-Therapy™; (c) The Imperium™.

require any extra pieces of equipment to be assembled with the pump before they can commence insulin therapy.

In addition to sharing the prefilled, pre-assembled simplicity of disposable pens, Imperium also has the therapeutic advantage of being an insulin pump. It comes supplied with a preset basal rate for continuous insulin infusion. On-demand bolus delivery is available to the user via a simple push of the button. Unlike with other insulin pumps, no complicated menu is required for bolus delivery.

Imperium is also capable of being a smart device, with the integration of Bluetooth LE connectivity paving the way for advanced informatics. Patients will be able to pair Imperium with an app on their smartphone. Authorised healthcare providers may also have access to data to help tailor the therapy to achieve glycemic control. The compact size of Imperium, as well as other features including water-resistance, makes it ideal for convenient, extended multi-day wear.

ADDING VALUE IN VACCINES

Today, vaccines are either provided in vials or standard prefilled syringes. Both of these packaging formats require the use of multiple pieces of equipment, and require multiple steps to prepare and inject the dose. The complexity of dose preparation is especially evident with lyophilised drugs that require around a dozen steps alone for reconstitution.

To comply with needlestick prevention laws in the US and Europe, most vaccine providers supply their prefilled products in a standard prefilled syringe with a luer fitting. While such products can minimise bulk during transportation and storage, they also place the burden of compliance for needlestick prevention onto the individual healthcare facility.

Needlestick safety products, such as needle guards, that are commonly used with vaccines must be purchased and attached separately onto the prefilled syringe by a healthcare worker prior to use. Their bulky size may interfere with the injection process, and increase the time required for preparation.

Upon the delivery of a dose, the operator must first remove the non-sterile needle from the body and then manually activate the safety mechanism to render it safe. Often, the used syringe is disposed with the safety mechanism un-activated, creating a



Figure 3: The Unifill Finesse 1 mL Standard syringe features an automatic and fully integrated retraction system.

risk of injury to those downstream. These factors can significantly increase the time and cost associated with vaccine delivery.

To overcome these and other challenges relating to the containment, shipment and delivery of vaccines, Unilife has created a complete, fully customisable portfolio of single and dual-chamber prefilled syringes. Most product configurations, including the Unifill Finesse 1 mL Standard syringe (see Figure 3), feature an automatic and fully integrated retraction system enabling operators to control the speed at which the needle is withdrawn directly from the body into the barrel to virtually eliminate infection risks associated with needlestick injuries or aerosolisation (blood splatter).

Dual-chamber systems with ventless, one-step reconstitution are also available with either staked, retracting needles or standard luer fittings. Amongst an array of customisation options, Unilife has created a proprietary telescoping plunger rod that significantly reduces product size to minimise shipping and storage costs.

With Unifill syringes being strongly user-preferred and accepted, pharmaceutical companies are able to leverage these feature and functionality advantages to further showcase the value of their vaccine brands against the competition.

ADDING VALUE IN AUTO-IMMUNE DISEASES

Many therapies targeting auto-immune diseases use disposable auto injectors. Whilst having some advantages over prefilled syringes including automatic dose delivery and the hiding of the needle, disposable auto injectors are commonly associated with number of challenges for both the patient and the pharmaceutical provider.

For pharmaceutical companies, there are additional costs to purchase and ship these bulky, single-use systems. Compared with a standard prefilled syringe, the cost per injection to utilise a disposable auto injector can increase by five to ten times or more. With most disposable auto injectors also having similar features and functionality, opportunities to utilise the device for brand differentiation are also minimised.

Auto injectors are primarily designed to inject doses of up to 1.2 mL in volume during a timeframe no longer than 15 to 20 seconds. Drugs which are unable to be formulated to suit delivery via a standard hand-held auto injector will typically require either injections to be given more frequently, potentially reducing brand preference rates, or require the transition to other device formats such as wearable injectors.



Figure 4: LISA is the world's first platform of smart, reusable and fully customisable auto injectors.

For self-injecting patients, disposable auto injectors have been linked with a range of user difficulties including limited portability, the extensive wait required for a biologic to warm to room temperature to minimise discomfort, pain associated with the speed of injection, and a lack of audible, tactile and visual indicators to confirm dose delivery.

To overcome these customer and patient unmet needs, Unilife has created LISA the world's first platform of smart, reusable and fully customisable auto injectors (Figure 4). Able to be used hundreds of times before replacement to minimise the cost per dose over a multi-year period, Unilife smart reusable auto injectors enable users to select the speed of injection to minimise potential pain or discomfort. Designed for use with Unifill prefilled syringes, the devices also enable safe, needle-free disposal. Capable of being integrated with Bluetooth LE connectivity for data informatics, the devices enable real time and historic access to data to support patient monitoring and compliance. A range of customisation features are available including a touchscreen display, pre-injection drug warming and RFID / NFC tag readers to check factors including drug expiration.

SUMMARY

The selection of a device platform by a pharmaceutical company should not only be based on how simple it is to customise, commercialise and use. As a preferred innovative device will ultimately play a significant role in the approval and commercial success of a target therapy, pharmaceutical companies should carefully consider how a device manufacturer can serve their long-term requirements with speed, agility and reliability.

In addition to having world-class, US-based manufacturing facilities and unparalleled innovation credentials, Unilife employs a dedicated team approach to customer programs. This approach enables Unilife to be fully responsive to a customer's needs in real-time, and encourages a close and collaborative relationship between the respective project teams. Unilife has also developed a company structure and culture that is highly customer-centric. Each project team that is established for a customer is composed of engineers, scientists and other experts from the drug delivery industry.

Unlike other companies where the business is predominantly based around materials or commodity components, Unilife was created from the ground up as a developer, manufacturer and supplier of sophisticated injectable drug delivery systems. It has a deep understanding of primary container technologies, and how they must be integrated into the effective production and functionality of a drug delivery system. From a customer perspective, this translates into having in Unilife a partner that has the expertise, processes and capabilities to take full responsibility for all aspects of the device and its integration within the overall drug-device combination product.

With Unilife also having a broad portfolio of injectable drug delivery systems, the company offers the neutrality to help pharmaceutical customers determine whether a particular molecule is best suited for use with a wearable injector, prefilled syringe, auto injector or a combination of two or more platforms. Unilife is ready to serve pharmaceutical customers under long-term partnerships to enable and enhance the delivery and commercial success of their injectable therapies.

Pre-filled,
Pre-assembled,
Ready-to-Inject.

Peel,
Stick,
Click.



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Wearable Injectors

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These products have not yet been evaluated by the FDA