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FORMULATION DEVELOPMENT AND DRUG DELIVERY: JOINED AT THE DEVICE

In this article, Julie Cotterell, Marketing Manager at Owen Mumford Pharmaceutical Services, discusses the major factors at play driving the direction of innovation in the subcutaneous drug delivery space, with a particular emphasis on the push towards patient self-administration.

The growth of the parenteral drug-device combination product market has been fuelled by a number of driving factors over the last couple of decades, in particular, longer life expectancy and the associated need for a greater number of patients to practise self-administration, as well as the increase in biologics and biosimilars, which have now captured 10% of the total biologics market value in Europe, according to a 2020 report by IQVIA. This stimulus has been felt both on the formulation and the device design sides.

Propelled by these key drivers, formulation science has therefore been developing along a series of key trajectories including the needs to:

- Develop greater biologic stability
- Reduce injection pain and frequency
- Allow for larger volumes of injectate
- Diversify drug delivery as well as improve ease of use for patients.

GREATER BIOLOGIC STABILITY

Ensuring the stability of biologic formulations is a challenge that requires the consideration of a number of elements. Interactions between the formulation and excipients, the primary container, oxygen and light, as well as any exposure to high extrusion or shear forces, are just some factors that may affect stability.

One of the methods undertaken to achieve greater stability and better facilitate subcutaneous injection has been the development of new excipients. However, use of these excipients presents a new set of challenges, such as interaction between the excipient and the silicon used to lubricate glass primary containers. Recently, there has been significant innovation in this area, from novel glass coatings to enhance stability to the use of innovative plastic primary containers that aim to minimise protein aggregation in biologics caused by silicon.

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Extending shelf life beyond the typical two-to-three-year range with post-launch stability studies can provide a significant commercial advantage. While storage at below room temperature is an option to extend shelf life, this route relies on patients remembering both to keep their drug refrigerated and to remove it before use. This is especially important in the case of biologics, where low temperatures increase viscosity, making the injection potentially more painful. Additionally, there are implications in the supply chain

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where cold chain conditions may be required for these products. With all new excipients, it is therefore critical to be aware that solving one issue may well cause others elsewhere – only an holistic approach can truly benefit development.

INJECTION FREQUENCY AND THERAPY ADHERENCE

As patients are increasingly enabled and encouraged to self-administer their medication in the home, the focus on patient convenience has also heightened. As a consequence, reducing injection frequency has become an area of focus for the industry, seeking to provide increased patient convenience and thereby improve therapy adherence. As a result, various novel drug-device combination products, including long-acting and extended-release formulations, have been developed. An increased focus on the patient experience – especially for those who self-administer – earlier in the drug development process provides a more patient-centric approach with wide-ranging benefits, including patient reassurance, comfort, convenience and usability. Regulatory pressure is also providing a significant push in this direction.

Increasing drug viscosity can also help to reduce injection frequency, but can have implications for administration – the needle length and gauge may have to be adjusted, there may be increased pain on injection and there may be an increase in the required injection time or device-hold time that may be inconvenient or even impossible for the patient to manage. Furthermore, there is the constraint posed by suitability and compatibility of the selected drug delivery device with the formulation.

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LARGER VOLUME PLATFORM DEVICES

In recent years, there has been a move from 1 mL up to 2 mL injectate volumes, and some exploration of 3 mL and higher, for subcutaneous delivery to reduce injection frequency. New excipients are also being trialled to enable the administration of larger volumes, thus reducing frequency of delivery. These may in turn permit the administration of >2 mL volumes and therefore require larger syringe sizes. Having a platform device that can easily accommodate both 1 and 2.25 mL prefilled syringes, as well as a variety of fill volumes, is a distinct advantage and allows flexibility throughout both development and commercialisation. Autoinjectors that have a two-phased, independent needle insertion and dose delivery can provide an improved and more consistent patient experience during the administration process, even for volumes up to 2 mL.

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DIVERSIFICATION

Greater choice of delivery device allows formulation experts to explore a variety of options – from formulation changes in early clinical studies to the creation of a range of differentiated products, each providing their own tangible patient benefits. The range of subcutaneous delivery devices is broad, running from safety devices for prefilled syringes to disposable and re-usable autoinjectors, through to wearable injectors, each of which may also have the capability to add connectivity and thus enable the transfer of key patient data and monitoring of therapy compliance. In addition to this, giving the patient choice of delivery method and device can help increase patient confidence and reassurance, positively impacting compliance to their therapy regimen.

While wearables have attracted a lot of attention, they are not yet mainstream, except in diabetes treatment. Challenges remain within formulation development that need to be addressed for successful adoption of wearables. However, the outlook for wearable devices is positive, as they have strong potential to provide a more convenient and comfortable means to deliver therapies to patients.

EASE OF USE

The need to simplify the use of devices to facilitate patient self-administration sometimes finds itself at odds with the technological potential of new devices. On the one hand, there is the emergence of connected devices, which are designed to help improve patient therapy adherence through better support and enabling monitoring by healthcare providers, while on the other hand, there is a trend towards more complex devices with additional features, such as variable injection speed and depth settings. However, the need to keep complex features and user steps to a minimum is paramount, as devices need to be simple and intuitive in order to both minimise user errors and encourage adherence. Simpler, more streamlined

devices that focus on the functionality needed for effective drug delivery, such as efficient end-of-dose indicators, are instead more likely to prove successful on the market than those featuring over-engineered features that, in practice, may confuse patients more than help them.

A MORE SUSTAINABLE FUTURE

Formulation and drug delivery device design and development are inextricably coupled and must respond to the same drivers, so it is unsurprising that the same trends are driving innovation on both fronts. Taking a holistic view of device and formulation right from the design and development stage is critical to ensure positive outcomes from both a commercial and a therapeutic perspective. Finally, sustainable design and development of devices have become increasingly important over the last decade, with governments, regulators, patients and consumers all calling for the industry to "go green". As such, mitigation of environmental impacts relating to manufacturing and waste products, and formulations with a less frequent dosing schedule are becoming increasingly popular options.

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ABOUT THE COMPANY

Owen Mumford is a major healthcare company and device manufacturer that commercialises pioneering medical products in its own brand and custom device solutions for major pharmaceutical and diagnostic companies. Owen Mumford's goal is to enhance access to diagnostics, encourage adherence to treatment and reduce healthcare costs, making a world of difference to a world of people.

ABOUT THE AUTHOR

Julie Cotterell is Marketing Manager at Owen Mumford Pharmaceutical Services and has over 20 years of sales and marketing experience in regional, national and global roles. She has a wealth of knowledge across several different aspects of drug delivery and the associated devices, with a particular interest in bringing products to market that can allow patients to be treated as simply and effectively as possible. Before joining Owen Mumford in 2018, Ms Cotterell worked for both pharmaceutical and medical device companies, including Baxter, BD and Smith & Nephew.

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