PEER REVIEWED

Designing Smart Integrated Drug Delivery Systems

Being diagnosed with a chronic condition is not easy. Whether it is diabetes, haemophilia, rheumatoid arthritis or multiple sclerosis, a patient is sure to begin a lifelong journey of care. After the initial shock of diagnosis has worn off, patients may experience a sense of relief that the cause of their health issues has been found. But many will respond with deep-seated emotions, such as anger or depression. The need to adhere to a regimen of treatment may be met with denial, fear or anxiety.

While adjusting to their new normal, patients around the world with chronic diseases are also seeking freedom from frequent doctors' visits, opting instead to self-administer their critical medications at home. This trend is emerging alongside another: an increase in new biologic and biosimilar medicines for the treatment of many autoimmune diseases. In fact, the QuintilesIMS Institute predicts that biologic treatments for autoimmune diseases will continue to see increasing usage across geographies, and spending on these therapies will reach $75–90 billion by 2021. In addition, biosimilars will be available for several leading autoimmune products by 2021, potentially allowing wider use of these medicines.[1]

As the industry shifts to be more sensitive to patient needs, and to activities to improve overall outcomes, the notion of in-home self-administration presents an opportunity to improve the overall patient experience, but creates the challenge of complying with described treatment regimens. This is where an injectable medicine's delivery system can help patients achieve their self-administration goal by making it a less painful, more streamlined and simplified process. For most patients, an easy-to-use, integrated drug containment and delivery system can be key to enabling the consistent routines that bring about compliance with care plans. When delivery systems are intuitive and efficient, they stand a better chance of helping patients stick with their treatment protocol because the impact on their daily routines lessens.

Conversely, injectable drug delivery systems deemed inconvenient, intimidating or complicated can negatively affect a patient's emotional attitude and motivation to sustain adherent behaviour. And in many cases, looks count, too: discreetness of the drug delivery system can be very important to certain patients. Some new integrated delivery systems can make it easy and convenient for patients to self-administer injectable medications without calling undue attention to the administration process, creating distractions to others or prompting feelings of stigmatisation. Such a shift from a product-centric focus to a patient-centric focus can help biopharmaceutical and drug delivery system manufacturers design a product that helps encourage compliant behaviour.

Putting Patients First in Drug Containment System Design

No matter what type of delivery system is selected for a particular injectable drug product, there are several elements that must be carefully considered when designing a drug delivery system. The primary goal of any drug delivery system is to ensure that a patient safely receives the proper dose of a prescribed medication. In years past, if a delivery system failed or was used incorrectly, patient error was most often the culprit. While providing detailed instructions is important for any pharmaceutical manufacturer, failure to follow directions should be minimised by providing proper training to the patient and/or caregivers.

Now, the industry is rethinking that stance, and the priority is engineering improved usability into the drug delivery system to help enable patients to achieve better outcomes. In order to design a drug delivery system that meets the needs of both the drug and the patient, the pharmaceutical manufacturer and its packaging and delivery system partner must consider the interface between the drug, container, delivery system and patient.

Understanding Patients Informs Usability

Effective drug therapy requires more than simply having an effective molecule. Rather, it is the combination of a safe drug within a suitable container and/or delivery system, as well as an understanding of patient needs as they relate to administration. Drug manufacturers should take into account four main facets of this integrated drug delivery approach that, when planned early in the development process with a packaging and delivery system partner, can lead to better outcomes:

Primary Container Format – The selection of a drug's primary container is an important consideration for drug efficacy and stability. Vials may be necessary for initial use during the drug development stages, but a syringe or cartridge system may provide a desirable solution for the patient when the medicine reaches the market. Custom containment systems may also help to differentiate the product, and should be considered early in the development process.

Drug/Container Compatibility – Hand-in-hand with the type of primary container is making sure the container material can be safely and effectively paired with the injectable drug product. Is the elastomeric material compatible with the drug? What are the levels of extractables and leachables? Will a barrier film

or coating be required for the elastomer? Choosing the proper drug container material can help prevent chemical incompatibility issues that could impact a drug's purity, stability or efficacy. It is also important to explore all of the available options for containment materials. While glass is suitable for many pharmaceutical products, high pH drugs or otherwise sensitive drug products may be incompatible with glass vials or syringes; therefore, it may be beneficial to consider containers made from alternative materials such as cyclic olefin polymers. The filling, handling and secondary assembly processes must also be considered as an integral part of providing the overall delivery system.

Container/Delivery System Interface – Once the primary container system has been selected, efforts must be made to ensure that it works with the delivery system. Dimensional tolerances and functionality should be tested to ensure proper activation and gliding forces. If the interface between the primary container and the delivery system is not effectively understood, the performance of the combined system may suffer. For example, when considering the use of a glass prefillable syringe in an auto-injector, manufacturers must ensure that the stress placed on the glass does not cause breakage or that the force in the auto-injector is enough to overcome variability in dimensions, functional performance and siliconisation effectiveness to ensure complete dosing.

Patient Interaction – Perhaps the most essential consideration is how the patient will use the drug delivery system. Even the most innovative drug can only provide the appropriate therapeutic benefit if it can be delivered effectively and the patient adheres to the necessary treatment regimen. Simply designing a drug delivery system that patients/users "can" use is no longer sufficient. Delivery systems should be designed in a way that encourages patients to want to use them. This starts from a thorough understanding of patient needs, including the fact that these needs may change during their treatment journey. Human factors analysis may be helpful here and can yield significant insight into patient behaviours, motivations and needs.

In addition, there is increasingly a fifth element to be considered that involves the potential for drugs to be effectively prescribed and reimbursed. With increasing costs for many modern biologic drugs, patient access may be determined by whether their insurance plan will cover the costs of the medicine.

Developing Smart Delivery Systems

Technology is a ubiquitous part of our culture, and drug delivery systems are following this trend. This is especially true for self-administration systems that can incorporate electronics to deliver doses at specific intervals and connectivity that allows patients and providers to track adherence via smartphone apps. Far removed from a vial and syringe in a doctor's office, today's advanced drug delivery systems are complex pieces of technology that can incorporate

innovative and intuitive features that can make it easier for patients to self-administer critical medications.

However, this shift has created an interesting challenge: while self-administration technology grows more complex, it must easily integrate into a patient's life. Irrespective of delivery features, drug delivery system manufacturers must ensure a number of qualities are present to bring value to their pharmaceutical partners. Key to this mission is creating technology that patients want to use by providing drug delivery systems that are:

- **Less painful:** Many drug delivery partners are developing self-administration systems that minimise discomfort. For example, using a large-volume injector can help to address the issue of discomfort during self-administration, as they can mitigate perceived pain with lower flow rates (higher flow rates are often associated with pain).

- **Easy to use:** Regardless of how innovative a delivery system is, it must be simple enough for anyone to use successfully. Arthritis patients, for example, may have limited dexterity, which inhibits their ability to use the delivery system. Through rounds of patient testing, manufacturers can ensure the platform is user-friendly.

When delivery systems are intuitive and efficient, they reduce the impact on patients' daily lives, increasing the potential for optimum adherence, which, in turn, delivers the kind of platform pharmaceutical partners need to market their drug.

Driving Innovation and ROI

As we have seen across all industries, new technology can become obsolete quickly. Pharmaceutical companies are relying on their drug packaging and delivery partners to remain continuously innovative and design integrated drug delivery systems that address the swift adoption of new technology. This can be achieved by working with pharmaceutical partners to create a new delivery system or adapting existing systems to address new technological advances.

Wearable drug delivery technology is a good example of how drug delivery technology providers continue to stay ahead of the curve. When originally introduced, wearable injectors combined the drug with the delivery system to automatically deliver the therapy. They dramatically reduced mistakes by ensuring patients received an accurate dosage at the time they needed it. But how could they be improved? By making wearable drug delivery systems compatible with smartphone applications, the technology became even more powerful. Now, patients can easily track dosage history, which can be analysed and shared with physicians, who can better understand where patients are in their journey to offer the most complete care.

To that end, drug delivery system manufacturing rosters now include scientists, software developers and engineers to make sure the self-administration systems are in sync with the latest technological advances. Many drug delivery systems will be connected to the Internet of Things (IoT), and companies and their packaging partners are leading the way to bring meaningful features to the patients they serve.

It is critical that these innovative efforts result in demonstrable return on investment (ROI) for biopharmaceutical companies, as they have to show patients, insurance companies, healthcare professionals and sometimes regulatory agencies that their drug is not only effective, but provides value. More and more, biopharmaceutical companies – which have less time resources to take contract manufacturing in-house – are relying on delivery technology partners to help them become market differentiators. By developing integrated drug delivery systems that promote accurate dosage and encourage greater compliance, greater potential exists for reduction in long-term healthcare spending for everyone involved.

Partnering for Patients

Patients start their journey with an initial diagnosis, but they travel a long road with a chronic condition. Pharmaceutical and delivery systems manufacturers must begin product development with that in mind, and create systems and options that will not only help patients learn to care for their condition, but also comply with their prescribed treatment regimens throughout their course of care.

To best create patient-centric systems, biopharmaceutical manufacturers should seek packaging and delivery system partners that can apply proprietary technologies, manufacturing excellence and patient understanding to their drug products and the products' delivery and administration systems. Such partnerships will help drug marketers offer successful, integrated solutions, benefitting manufacturers, clinicians and patients alike, while helping to ensure optimum adherence and improving patient outcomes. Because after all, isn't that the shared goal of everyone involved?

REFERENCES

1. QuintilesIMS Institute. Outlook for Global Medicines through 2021: Balancing Cost and Value. December 2016.

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