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ADVANTAGE, PHARMA: PARTNERING WITH PACKAGING & DEVICE COMPANIES EARLIER IN THE DRUG DEVELOPMENT CYCLE

In this article, Tibor Hlobik, Director, Global Marketing, Prefillable Syringe Technologies, and Kevin Cancelliere, Director, Pharmaceutical Delivery Systems Marketing, both of West Pharmaceutical Services, Inc, discuss how and why early consideration of primary packaging and drug delivery devices in pharmaceutical product development can bring benefits to all stakeholders, including patients.

Drugs, understandably, are the primary focus of research and development for pharmaceutical and biopharmaceutical companies. But with increased regulatory focus on quality in drug packaging and delivery systems, pharmaceutical manufacturers are considering the importance of containment systems ever earlier in the drug development process. Forward-thinking companies build in time for early collaboration with packaging and delivery system partners during the lengthy development process. This better positions the injectable drug to serve the needs of both the manufacturer and the patient.

> "The most successful recent blockbuster drug launches have involved specialised products that are launched to meet highly unmet medical needs in areas, including diabetes, multiple sclerosis, osteoporosis, psoriasis and schizophrenia. Each of these new drugs had one thing in common: they were launched with alternative delivery methods"

Often, one of those needs is maximising patent protection time. Research and development for a new biologic drug product can typically take as long at 15 years and cost as much as US$1.2 billion (£0.8 billion). So when the drug product reaches the market, the originator may have only a few years remaining on the patent.

That's where the expertise and experience of the packaging and delivery system partner can help – earlier in drug development – to save precious time the pharmaceutical company has for exclusive rights under patent. Typically, drug manufacturers consider drug packaging and delivery systems only during the final stages of development. If the drug product cannot be stored effectively or reacts chemically with the containment materials, or if the system does not function well with a high-viscosity drug or is not a good fit for the intended patient population, it can be a costly issue for the manufacturer. Considerations related to dosing volume, delivery technique and frequency, and type of delivered system (such as an auto injector), should all be taken into account at an early stage to ensure optimum speed-to-market and opportunity for success.

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EARLIER TESTING, BETTER RISK MITIGATION

Collaborating with a single partner with diverse expertise in primary packaging, delivery systems, custom design and analytical testing early in the drug process can help at a variety of stages. For example, packaging manufacturers that also provide analytical laboratory services can offer product recommendations for the latest alternative technologies and provide prescreen stability work early in the process to ensure that the containment materials do not react with the drug product.

Many biologics, by their very nature, do not respond well to glass containment, which can result in higher levels of inorganic leachables, protein aggregation or the risk of glass delamination. To achieve the best possible patient outcomes, pharmaceutical companies developing complex and sensitive biologic or biosimilar injectable therapies must consider how the drug product will interact with the primary container, the delivery system and the patient to help ensure compliance to prescribed regimens and loyalty to specific brands. The most successful recent blockbuster drug launches have involved specialised products that are launched to meet highly unmet medical needs areas, including diabetes, multiple sclerosis, osteoporosis, psoriasis and schizophrenia. Each of these new drugs had one thing in common: they were launched with alternative delivery methods.

By partnering with a component manufacturer early in the drug development process, pharmaceutical manufacturers can identify and mitigate many of the risks associated with poor containment selection. Flexible containment solutions that use the same materials for drug contact, but in a variety of configuration options that aid in stability and delivery from discovery through commercialisation and drug lifecycle management, may help achieve better patient outcomes.

ENSURE DRUG STABILITY AND LIMIT LEACHABLES FORMATION ASSOCIATED WITH CLOSURES

Every company involved in packaging injectable products, especially sensitive and biologic drugs, is concerned about long-term stability and the impact of potential extractables on drug quality and patient safety. The most frequently asked question is, "What is the acceptable level of leachables over the shelf life of my product and associated risk to the patient population?"

Figure 1: NovaPure® plungers with FluroTec® film provide high reliability for prefilled syringe systems.

By applying barrier films to stoppers, plungers and cartridge components, an elastomer closure's performance can be improved. Such films can help reduce the risk of interaction between the drug and container closure system and protect the drug from contamination. FluroTec® film provides an effective barrier against organic and inorganic extractables, minimising interaction between the drug and the closure while maintaining container closure integrity. The fluoropolymer film reduces drug product absorption and adsorption, an important benefit for maintaining the strength and shelf life of most drugs. In addition, the low surface energy of FluroTec film, in combination with a lubricious coating, such as B2-Coating, eliminates the need for added free silicone oil on the component, eliminating one potential source of particulate contamination.

A NEW WAY TO MEET INCREASING QUALITY REQUIREMENTS AND DEVICE COMPATIBILITY

Quality by Design (QbD) promotes understanding of the product and manufacturing process starting with product development. When designing and developing a product using QbD principles, manufacturers must define desired product performance and identify Critical Quality Attributes (CQAs). The product and process is then designed to meet those product attributes, which leads to understanding the impact of material attributes and process parameters on the CQAs and identification and control of sources of variability. As a result of this knowledge, a manufacturer can continually monitor and improve its manufacturing process to assure consistent product quality.

As market demand for higher quality and patient need for self-injection with auto injectors have evolved, demand for a high-quality plunger has grown. Using QbD principles, West developed its NovaPure® plunger (Figure 1) with FluroTec film for prefilled syringe systems to provide high reliability for break-loose and glide force, dimensional accuracy, sub-visible and visible particulate control, and low parts per million (ppm) defect attributes. The optimised functional performance for NovaPure plungers can provide improved rate of injection times and consistency when used in conjunction with 1 mL long syringes and an auto injector system.

POLYMERS GAINING ON GLASS

Examination of potential fundamental incompatibilities between drug formulations and container closure systems, has led manufacturers to explore and adopt alternative primary container materials such as cyclic olefin polymers (COPs). These can help assure optimum stability during a drug product's shelf life.

Cyclic olefin polymers may offer a safer, more effective and reliable alternative to traditional glass. Because COPs can be moulded to a variety of shapes, they can provide adaptability to different administration forms (e.g. infusion to injection to self-administration) throughout the product's lifecycle. Such choices early in development may aid decisions later in the manufacturing cycle. COPs offer improved dimensional tolerance and design flexibility, so innovative container/device combinations can be considered to help optimise overall system design based on the needs of the patient.

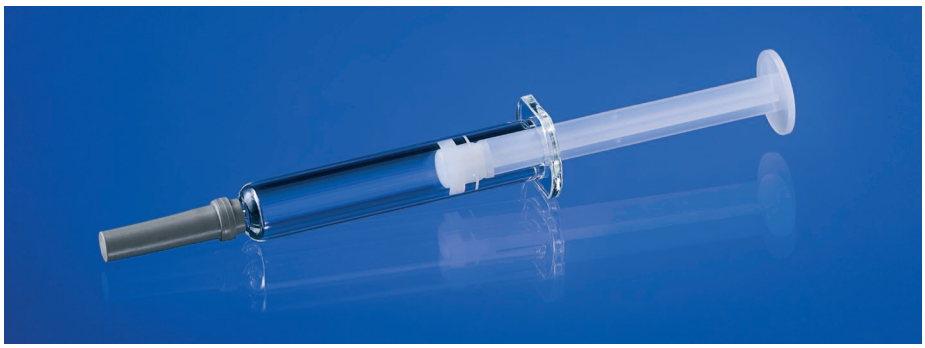

Figure 2: The Daikyo Crystal Zenith® 1 mL Insert needle syringe.

Companies challenged with multiple containment needs for drug lifecycle management strategies can work closely with the partner to match technology, collaborate during development and ensure primary container compatibility with the drug and device for best patient outcomes. Many biotech and sensitive drug products have unique requirements, and polymer systems provide key solutions for patient safety and compliance. There are a variety of products on the market that can help mitigate these risks, including insert needle prefillable syringes, such as the Daikyo Crystal Zenith® 1mL Insert needle syringe (Figure 2), which may be required for a drug product with metal and silicone oil sensitivities.

Another consideration in this process is the need to integrate primary containers into drug-device combination products. As patients take a more active role in their individual healthcare, and the administration of injectable drug products moves from hospital to in-home setting, there is a greater need to provide easy-to-use delivery systems or combination products that assure safe and reliable self-administration. This may include the use of prefillable syringes, which help in dosing accuracy and minimise errors when compared with a vial and disposable syringe format.

AUTO INJECTORS, CARTRIDGE-BASED SYSTEMS HELP PATIENTS COPE

There has also been an increase in the use of disposable auto injector systems, which aid dosing convenience, and may help reduce patient fear because they include safety features that hide the needle before and after injection.

Another trend allowing for even greater patient convenience is the use of cartridge-based systems. These may include pen injectors for frequently administered products, as well as large-volume electronic wearable injector delivery systems that can offer either less frequent administration or conversions of products from intravenous to subcutaneous administration.

West's SmartDose® electronic wearable injector is designed to deliver higher fill volumes of injectable drugs over an extended period of time, making it easier for patients to self-administer medication and encouraging compliance with prescribed treatments.

EARLY COLLABORATION, MORE OPPORTUNITIES

Between 2003 and 2014, the number of top selling biologic drugs has grown from one product to five. Biologics and biosimilars have seen continued growth at a pace that exceeds other drugs in the market and in the pipeline. Through 2018, biologics spending will continue to grow faster than medicines overall, driven by innovation.

It is important to note that biologics make up roughly one-third of the late-stage drug pipeline. Companies developing these specialised drugs can hedge their bets for success by selecting a packaging partner that can accommodate the complexities biologics sometimes introduce to the process.

West is proud to partner with our customers to anticipate their packaging and drug delivery needs and bring them value-added solutions to remain competitive in today's complex healthcare landscape.

FluroTec® is a registered trademark of West Pharmaceutical Services, Inc, in the United States and other jurisdictions. NovaPure® is a registered trademark of West Pharmaceutical Services, Inc, in the United States and other jurisdictions. SmartDose® is a registered trademark of Medimop Medical Projects Ltd, a subsidiary of West Pharmaceutical Services, Inc. West seeks partners for its SmartDose injector technology platform. This platform is intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical/biotechnology company.

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ABOUT THE AUTHORS

Tibor Hlobik, Global Director, Marketing for PFS Technologies

Tibor Hlobik has worked within the pharmaceutical packaging industry for over twenty-five years in areas of research and development, corporate quality, technical services and marketing primarily at West Pharmaceutical Services. He has extensive knowledge and experience with prefilled syringe systems and cartridge based solutions, and related technologies. Currently in his role as Global Director, Marketing for PFS Technologies at West Pharmaceutical Services, Tibor is responsible for defining new market requirements, launching new products, supporting business development plans, and overall execution of global marketing strategies for West.

Kevin Cancelliere, Director of Marketing, Pharmaceutical Delivery Systems

Kevin Cancelliere joined West Pharmaceutical Services in January 2013 as Director of Marketing, Pharmaceutical Delivery Systems. Kevin brings almost thirty years of broad operational and strategic marketing and sales experience to this position. He comes to us from Vicept Therapeutics where he was Senior Director, Project Management for an investigational drug for the treatment of Rosacea. Prior to Vicept, Kevin was the Senior Director, US Marketing at Wyeth Laboratories. Kevin holds a BS in Biology from De Sales University and a Masters in Biochemistry from Thomas Jefferson University.

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Patient safety should be driving your selection of drug packaging components. West's NovaPure® components were designed to help ensure the efficacy and safety of your drug. With West, you have a partner by your side from discovery to the patient.

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