TRENDS SHAPING THE DYNAMIC MARKET FOR PARENTERALS

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Demand for parenteral drugs continues to increase as the overall drug market expands and new therapies for both chronic and rare diseases enter the pipeline. Manufacturers are faced with increasing complexity, not only because of the drug substances but also due to formulations, patient-centric delivery technologies, and regulatory requirements, which are all further complicated by abbreviated development timelines.

CONTINUED MARKET EXPANSION

Parenteral administration is the second most common type of drug delivery after oral solids and liquids. Over the last several years, parenteral drugs have accounted for approximately 40% of new molecular entities approved by the U.S. Food and Drug Administration each year.[1] In 2018, there were nearly 500 parenteral drugs in the pipeline.[2] The global market for parenteral drugs was estimated to be $451 billion in 2019 and to be expanding at a 6% compound annual growth rate (CAGR)[3] to reach a value of $802 billion by the end of 2029.[2] The rising prevalence of chronic illnesses and the growing importance of biologic drugs are key drivers of the rising demand for parenterals.[3]

The large volume parenteral (doses of 100 mL or more) subsegment is also expanding at a compound annual growth rate (CAGR) of approximately 6% through 2025.[4] Specific drivers for the growth of these parenteral drugs, the bulk of which are nutritional and electrolyte formulations (infusions of amino acids, mannitol, dextrose, lactated Ringer's injection, Ringer's injection, sodium chloride) are increases in geriatric and pediatric patients, as well as people suffering from cancer and other chronic illnesses.

With respect to parenteral drug packaging, the global market was valued at $9.86 billion in 2017 and is projected to expand at a CAGR of 4.8% through 2028.[5] Prefilled syringes and cartridges accounted for more than 35% of the market and are expected to increase compared with vials, bags, and ampoules.

GROWING PERCENTAGE OF BIOLOGICS

One of the key drivers for growth in the parenteral drug market is the many advances being made with respect to biologic drugs, from monoclonal antibodies to next-generation cell and gene therapies. These drugs have proven effective in treating many chronic illnesses and rare diseases. Due to their large size and other physicochemical properties, biologics to date have required parenteral administration. In 2018, monoclonal antibodies dominated the parenteral drug market, accounting for 20% of sales.[2]

GENERICS AND BIOSIMILARS HAVING AN IMPACT

Both popular small molecule and biologic parenteral drugs will be losing patent protection over the next several years, with more than 30 drugs likely to see generic or biosimilar competition. In fact, the global small molecule injectable drugs market is predicted to expand substantially from 2017 to 2025 due to growth in generic injectables, which is outpacing that of innovator drugs.[6]

Biosimilars are in particular increasingly important in the parenteral drug market. As greater numbers of these drugs are approved in the United States and around the world, their acceptance by physicians, patients, and insurers is increasing. Contract development and manufacturing organizations (CDMOs) are likely to experience the greatest impact from this trend, as many generics and biosimilars are outsourced to achieve greater cost efficiencies.

INCREASING IMPORTANCE OF ORPHAN DRUGS AND EMERGING BIOTECHS

Two trends having profound impacts on the parenteral drug market are interrelated. The first is the transition across the pharmaceutical industry from a focus on the development of blockbuster drugs to an emphasis on therapies that treat rare diseases, in part driven by new legislation encouraging the development of orphan drugs. The global market for drugs that are designed to treat rare diseases and receive orphan drug designation is expected to expand at a CAGR of 11% from 2018 to 2026, reaching a value of $262 billion.[7] This new paradigm has created opportunities for many small and emerging pharma and biotech companies to bring to market highly specialized medicines for targeted, smaller patient populations.

These smaller firms typically have limited resources and rely heavily on CDMOs for support throughout the entire drug development and commercialization process. At the same time, the switch to orphan drugs has created challenges for CDMOs due to the often small volumes required for these specialized treatments. Manufacturing of these products must be achieved at a smaller scale and typically under accelerated timelines in a manner compliant with the current good manufacturing practice (cGMP).

EMPHASIS ON PATIENT-CENTRIC PRODUCT DEVELOPMENT

The growing importance of patient-centric product development has not escaped the parenteral drug segment. If anything, manufacturers of parenteral drugs have been leaders in the development of novel delivery methods specifically designed for ease of use and convenience, both for caregivers and patients that self-administer their own medications.

The global market for self-injection devices was valued at $3.7 billion in 2017 and is projected to expand at a CAGR of 13.5% to reach $11.3 billion by 2026.[8] Prefilled parenteral drug-delivery devices in development include wearable, smart, needle-free, single-use, and combination products and come with a variety of packaging options, all designed to offer flexible dosing options and increase medication adherence.[9]

In addition to continuous improvement of prefilled syringes, pens, and autoinjectors for subcutaneous (rather than intravenous) delivery, companies are beginning to leverage digital solutions, such as mobile apps and prescription digital therapeutics. Wearable injectors, as well as autoinjectors, have the potential to help with the administration of high-viscosity and large-volume drugs. The wearable injectors segment is predicted to grow at a CAGR of 20% from 2018 to 2026.[8]

THE CHALLENGE OF VISCOUS FORMULATIONS

Some of the advances in injector device technologies are driven by the growing need to deliver high-viscosity parenteral drug products in a comfortable manner.[10] Traditional spring-loaded injectors are no longer sufficient for these products. Some drugs, particularly biologics, can be highly viscous by nature. Other formulations are viscous because they are designed to be long-acting to reduce the frequency of required injections. In other cases, drugs initially formulated for IV administration are being reformulated to allow self-administration and can result in high-viscosity and/or high-dose products.

GREATER COMPLEXITY ACROSS THE BOARD

Both pharma/biotech companies and their CDMO partners are faced with increasing complexity across all aspects of parenteral drug development and manufacturing. In addition to the move to specialty drugs with targeted patient populations that

need patient-centric formulations and delivery options, companies are faced with more chemically complex molecules that can present synthesis/cell culture, analytical, and delivery challenges.

As personalized medicines represent a larger fraction of the pharma pipeline, clinical trials are also becoming more complicated. CDMOs must be positioned to support clients to not only overcome manufacturing challenges, but regulatory complexities, particularly within shortened timelines. They will need the flexibility to support both small- and large-volume manufacturing of a wide range of drug substances, including highly potent small molecule and biologic drugs, such as antibody–drug conjugates, as well as numerous formulation types and administration systems.

IMPLEMENTATION OF AUTOMATED MANUFACTURING SOLUTIONS

The increasing implementation of automated manufacturing solutions that leverage robotic technologies is one way that many parenteral drug producers are addressing the complexities they face. Automated systems significantly reduce human interactions with the product and process, thus reducing the risk of contamination. For highly potent/cytotoxic products, automated, closed systems also provide protection for operators and the environment.

Furthermore, automated processes are typically more efficient. Robots can be programmed to perform the same motion, exactly the same way every time, something that is not possible for humans to accomplish. They also enable the collection of large quantities of data that can be analyzed and used to make process improvements that lead to even greater productivity. Overall, automated processes are robust and efficient and lead to more consistent and higher-quality products.

QUALITY CULTURE AND CONTINUOUS IMPROVEMENT ARE ESSENTIAL

In the complex environment of sterile parenteral product manufacturing, a culture of quality and effective quality systems are essential for success. An appropriate quality culture includes a commitment to continuous improvement and an emphasis on designing quality into parenteral manufacturing processes from the start. The use of a quality-by-design (QbD) approach and compliance with requirements for parametric release are two key components of a successful and effective quality program.

CREATING A QUALITY LEADER

Grifols Partnership has decades of experience in the production of small molecule parenterals and has amassed extensive knowledge of the processes we use and the products we produce. Our experience includes conventional and orphan/rare disease drug projects at clinical to commercial scales.

As a business unit within a global pharmaceutical manufacturer, we also have access to financial, technical, regulatory, and other resources not readily available to standalone CDMOs, yet we are flexible enough to be an ideal partner for small and emerging pharma companies. Our collaborative and integrated project management brings together cross-functional teams that provide the highest standards of quality to our customers while helping to reduce or prevent potential problems that could result in unwanted delivery delays in getting products to market.

Notably, at Grifols Partnership, we have implemented a QbD approach to process development and enhanced our process-control capabilities. Our proactive approach to continuous improvement enables us to improve processes before any issues occur. We also have an established change management control system and have installed automation systems/technologies at both of our plants in Spain to facilitate manufacturing and maximize product quality and patient safety. Our high-quality performance is reflected by approvals in Europe for the parametric release of products. As a result, Grifols is established as a leader with the highest reputation for quality. P

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