Injectable Delivery

Market Trends in Injection Devices for Pharmaceuticals

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Improving the convenience and ease of administration of parenteral therapeutics is becoming a common strategy to augment product marketability in the biotechnology and pharmaceutical industry. Both the growth of the injectable market and increased competition in the industry have driven product improvements for healthcare professionals and patients. Injection devices and end-user aids that facilitate preparation, ease administration and ensure safety are increasingly prevalent in the marketplace. Because most injection devices are proven technologies that can be commercialised within one to three years, these systems are an attractive option for differentiating a product in a competitive marketplace. Despite the additional operational burden associated with introducing a device into the pharmaceutical business, companies are undertaking this endeavour to retain or gain market share in competitive environments.

The growth of devices in the pharmaceutical industry is evidenced by the stream of new devices that have entered parenteral drug markets worldwide and by significant technology advancements in those markets that have used injection devices for many years. Injection devices have been used commercially for the last 20 years in the diabetes, growth hormone deficiency and emergency medicine markets. Over the years that devices have been used for insulin and human growth hormone (hGH), drug delivery has become remarkably advanced. In these markets, all companies provide at least one device, and some companies offer as many as four devices; vials are a less common dosage form. The devices have undergone numerous generations of improvements. The most recent development for drug delivery is the European Medicines Agency (EMEA) and US Food and Drug Administration (FDA) approval for inhaled insulin, which will be the first biopharmaceutical product that is administered systemically by a non-invasive route of administration. As for drug delivery in new markets, devices for injection, product preparation and safety have been introduced into multiple sclerosis (MS), rheumatoid arthritis (RA), hepatitis, osteoporosis, haemophilia, reproductive health, anaemia, haemolytic disease, antithrombolytic therapy, and oncology markets in the last five years. Additionally, the types of devices being marketed by drug delivery companies to pharmaceutical companies are growing in diversity.

Injection Devices

Pen injectors have been widely used in the diabetes market for the last 20 years and in the hGH deficiency market for the last 10 years. These devices recently entered the reproductive health, osteoporosis and hepatitis markets. Pen injectors have typically been used for frequent self-administration of preserved multi-dose drug formulations requiring weight-based dosing. However, fixed dose and single use pens have recently been commercially marketed. Insertion of the needle and injection of the drug is manual with these systems. Pen injectors have historically been reusable devices that require the end-user to periodically replace the drug cartridge. Disposable pen injectors have been introduced more recently. These systems are supplied pre-assembled with the cartridge, and the entire device is discarded after the drug contents have been used. Pen injectors can accommodate liquid or lyophilised formulations, which is an advantage over some other types of devices that are limited to liquids. The newest developments in pen devices include the use of needle safety devices, automated needle insertion and injection, and electronics.

Auto-injectors, spring-driven systems that automatically inject the drug into the skin via a prefilled syringe or cartridge, have been co-marketed with drug products in the multiple sclerosis (MS), rheumatoid arthritis (RA), reproductive health, anaemia and oncology markets in the last five years. Reusable auto-injector systems have become particularly well established in the MS market; second- and third-generation auto-injectors have recently been commercialised. Reusable systems are a cost-effective option for frequently administered products. These auto-injectors require a significant amount of end-user manipulation to perform an injection, and the complexity of use has potentially limited their popularity. Current trends are towards
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single-use disposable auto-injectors. These systems have been used in the emergency medicine markets for over a decade, but have only recently entered the anaemia and oncology markets with therapeutic proteins. These systems are supplied pre-assembled with a pre-filled syringe containing the drug. They are inherently easier to use than reusable systems and can have integrated needlestick protection, which makes them flexible for use in clinical and home administration settings. Reusable systems are suitable only for self-injecting applications.

Needle-free injectors enable the administration of drug products without the use of a needle. A high-pressure gas or spring drives the drug product through a small orifice directly through the skin. To date, needle-free injectors have not made major commercial inroads into the injectable marketplace. The only needle-free devices marketed by the pharmaceutical industry are reusable systems in the hGH market. Reusable systems offer dosing and formulation flexibility but, as is typical of all reusable devices, they are more difficult to use than disposable versions. Single-use disposable needle-free devices have not yet been commercialised, but are in late-stage development by a number of companies for products in the haematology, MS, RA, and migraine relief markets. Most disposable devices in development are designed to be pre-filled and to give a single fixed dose. Historically, disposable needle-free technologies have been limited to liquid formulations, but recent developments include the ability to dose a lyophilised formulation using a dual-chamber cartridge.

Reconstitution Aids and Devices

Reconstitution of a lyophilised product prior to injection is an inconvenience that numerous pharmaceutical companies have sought to offset by the use of dual chamber syringe/cartridge systems or adaptors that enable needle-free reconstitution in vials. Such systems are now used in the MS, RA, hepatitis, oncology, and haemophilia markets with lyophilised products. Dual-chamber systems contain the diluent and powdered drug in the same primary container and enable mixing via a channel that connects the drug and diluent. These are available as pre-filled syringes or as pre-filled cartridges for use with an injection device. A variety of reconstitution aids are available to facilitate reconstitution of lyophilised drug products in vials. Vial adapters connect a diluent vial and product vial with a syringe, or a vial directly with a diluent syringe. Some adapters are pre-attached to the product vial and diluent syringe or have pre-attached needles. Recent developments include vial adapters for multi-dose formulations. Tools to assist the patient in removing caps on vials and syringe caps and/or handling needles have also been marketed. Some injection device companies have developed devices that enable reconstitution and automate injection, but none have been commercialised to date.

Reusable auto-injector systems have become particularly well established in the MS market; second- and third-generation auto-injectors have recently been commercialised.

Needlestick Prevention Devices

Since the US Needle Stick Safety and Prevention Act of 2001, which requires that healthcare professionals take appropriate measures to avoid accidental needlesticks, engineered sharps injury protection (ESIP) systems have been supplied with clinically administered drug products. Since this time, needlestick prevention devices have been commercially marketed with over a dozen pharmaceutical products in the oncology, hepatitis, RA, antithrombotic therapy, and haemolytic disease markets. These systems provide a mechanism to shield the needle after injection and prevent accidental injury. Manual systems, in which the healthcare provider manually places the protective guard over the needle, are becoming obsolete technologies with the introduction of passive systems. Passive devices activate the needle protection guard at the end of the injection without any action by the user.

Trends for the Future

The types of devices and aids that will be commercialised are increasing in diversity, and injection device companies are developing devices that overcome previous limitations and conventions. For example, a pen has historically been a manual,
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reusable cartridge-based system for preserved multi-dose products (liquid or lyophilised) with variable dosing, and auto-injectors were automated syringe-based systems for fixed-dose liquid formulations. Fixed-dose and single-use pens have recently been commercialised. New developments for pens include automation of needle insertion and drug delivery. Likewise, auto-injectors with manual needle insertion or variable dosing are now under development, and designs for systems with lyophilised formulations have been conceptualised. Various injection devices for delivery of viscous products are in development. There is also an evident trend from reusable to disposable devices. Insulin products transitioned to disposable systems in the 1990s, and product sales have since been shifting from the reusable to the pre-filled disposable systems. Since the year 2000, hGH, fertility, anaemia, oncology, osteoporosis, and hepatitis products have either transitioned to or been launched in disposable systems.

Injection devices have been typically used as life-cycle management tools in the pharmaceutical industry. A common life-cycle management scenario would be for a product to launch in a vial, transition to a pre-filled syringe, and then transition to an injection device. More first-time launches will be with devices, as new products entering a device-populated market are potentially at a disadvantage. An RA product launched in a pre-filled syringe with a device was available in 2001. In 2003, an osteoporosis product was the first to be launched as a pre-filled disposable pen without other types of conventional systems, such as vials or pre-filled syringes, available. Another product used this approach in the diabetes management market in 2005. In addition to these injection devices, the needlestick legislation has driven clinically administered products to be supplied with ESIP devices at launch.

Devices have been commonly commercialised by small drug delivery companies for general use with insulin or other products. The increasing prevalence of devices in the market can largely be attributed to co-marketing with branded drug products from the pharmaceutical industry, as the drug companies have a greater infrastructure for marketing to the target patient population. Companies that develop and commercialise numerous injectable products are also likely to develop device platforms that can be used for multiple drug products. This approach is the most operationally sensible and cost-effective, as it enables a company to leverage their technology for multiple applications. Companies with a long-standing history with devices have taken such an approach. Devices are also likely to undergo multiple generations of technology improvements.

Other indications of a market trend towards improved convenience and ease of administration are the transition from shorter- to longer-acting products with less injection frequency and the transition from lyophilised to liquid formulations, which have fewer preparation steps. Longer-acting products have been recently introduced in the insulin, growth hormone deficiency, anaemia, RA, dermatology, oncology and hepatitis markets, and products in the MS, RA, growth hormone deficiency and infertility markets have transitioned from lyophilised to liquid formulations over the last five years. These product improvements are often used in combination with devices, or devices are used to offset the disadvantages of lyophilised formulations or more frequent administration.

**Concluding Remarks**

Injection devices and preparation aids improve the injection experience, enhance compliance, and ensure safety. These systems are playing an increasingly prominent role in a range of competitive injectable markets. The growth and competitiveness of the injectable market is spurring extensive development of new and nth-generation devices that are overcoming previous drug delivery limitations and conventions. Conventional parenteral dosage forms such as vials will become outdated as devices become increasingly integrated with drug products.

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