Auto-Injectors: Technology Advances and Market Trends

The variety of auto-injector devices available on the market is expected to continue to grow over the next few years, with competition to meet requirements spurring innovation in new therapy areas.

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The market for automatic injection devices, or auto-injectors, is enjoying a period of rapid growth. In this article, we will discuss the user and business benefits that are driving this growth, the current state of the technology and the potential directions in which the market may move in the future.

An auto-injector may be described as a device which completely or partially replaces the activities involved in parenteral drug delivery from a standard syringe. Typically, these include removal of the protective syringe cap, insertion of the needle, injection of drug, and possibly removal and shielding of the used needle. In the context of this article, auto-injectors are considered as distinct from the class of multiple, variable dose pen injectors commonly used for insulin administration.

USER BENEFITS

Administering an injection is a process which presents a number of risks and challenges, both mental and physical. The use of an auto-injector can bring many benefits for the user and healthcare professional – these include the following.

Simplifying Self Administration

Patients often find that auto-injectors are easier to use than regular syringes as they simplify the injection process (see Figure 1); manual injections involve more steps than an auto-injector administration. Patients who use auto-injectors are often able to self-administer in the convenience of their home – indeed, some patients who would not be suitable candidates for a needle and syringe due to impaired vision or dexterity can use auto-injectors with ease. The use of auto-injectors may thus reduce the requirement for costly visits to clinics.

Reducing Anxiety

Needle phobia is managed well with an auto-injector, as the user does not see the needle and does not need to manually insert the needle into the skin. Many patients find the concept of inserting a needle more difficult than the pain of the injection itself.

Improving Safety

Needlestick injury prevention is a primary driver for companies and healthcare institutions to introduce auto-injectors. Many auto-injectors offer the additional benefit of needlestick protection to healthcare professionals. It is estimated that in the US alone, 69,000 injuries per year could be prevented (1). Nurses have the highest rates of injury, with relatively high rates also occurring in junior doctors. Many auto-injectors have passive, integral safety features which eliminate or greatly reduce the risk of injury.

Improving Compliance

Auto-injectors are designed to perform a standardised administration; they insert the needle to a specified depth.
and many ensure that the full dose is delivered every time. Drug delivery from an auto-injector is more controlled, and therefore likely to be more consistent, than a manual injection. Studies with pen injectors link patient convenience to improved patient compliance, particularly when motivation to follow the prescribed course of therapy is low (2). Auto-injectors may be custom-designed to overcome specific compliance issues related to drug administration, which may have benefits in demonstrating the efficacy of the therapy. Some auto-injectors have been designed to actively assist with patient compliance by reminding patients to take their medication at correct intervals and tracking the dosage (3).

BUSINESS BENEFITS

The use of a well-designed drug delivery device addresses not only the needs and desires of the user but also offers a number of business benefits; these include the following.

Meeting Customers’ Needs
In a competitive market, where users are in a position to dictate their preference, meeting user requirements is the key to product success. Many patients now play an active role in their treatment and if they do not like the method of drug delivery, they may request a change of therapy. Being able to offer a variety of drug delivery methods can increase the penetration of a product into the market.

Meeting Legislative Requirements
Following the passing of legislation in the US, the Occupational Safety and Health Administration (OSHA) has revised its standards to clarify the need for employers to select safer needle devices as they become available, and to involve employees in identifying and choosing the devices.

Creating and Protecting Market Share
The launch of a new drug product into an established market can be aided by using an auto-injector to provide product differentiation. As drugs become mature products, market share is likely to be eroded by competitors. This is particularly true for drugs that are coming out of patent protection and will be subject to competition from generics. In such cases, market share may be protected by supplying an auto-injector. A good example is in the market for the monoclonal antibody therapeutics used to treat conditions such as rheumatoid arthritis and psoriasis. Two established products, Enbrel® from Amgen and Humira® from Abbott Laboratories, are both now supplied in a disposable auto-injector device, as well as the regular pre-filled syringe.

Protecting Patients and Businesses from Counterfeiting
Although it is difficult to obtain precise figures, the US FDA estimates that worldwide sales of fake drugs exceed US$3.5 billion per year (4). If a drug product is supplied in a single-use, disposable auto-injector, it is afforded an extra layer of protection as the device itself will be difficult and costly to counterfeit. The provision of tamper-evident features in the design can help to make it difficult or impossible to gain access to the primary packaging without destroying the device.

DEVELOPMENTS AND TRENDS

Medical device manufacturers have been producing low-cost, re-usable devices for many years. Early applications included the administration of hormone replacement therapies, although these systems still required the user to draw the dose from a vial into the syringe before loading it into the device. As the benefits of auto-injectors became widely acknowledged, the requirement for higher volumes at a lower cost prompted manufacturers to produce devices from injection-moulded plastics. The first re-usable auto-injector, containing a pre-filled syringe of the anti-migraine product Imigran®, was launched by Glaxo in the 1990s. This was a ground-breaking device and allowed patients experiencing a migraine attack to self-administer a subcutaneous injection. These, and similar devices, are still being produced in large volumes and are frequently offered to patients who wish to administer their own injections. A variety of auto-injectors in development and currently on the market is shown in Figure 2.
Disposable, single-use auto-injectors have, for several years now, found application in the administration of emergency therapies, such as adrenaline for patients experiencing anaphylaxis or atropine for field use in the military. The use of an auto-injector in these situations has the clear benefit of rapid, simplified administration. Emergency devices typically have very simple, functional designs that achieve a high level of reliability in a critical situation. However, they are not necessarily designed to address needle safety — or indeed some of the softer user needs such as needle phobia.

A New Generation of Devices

More recently, several designs of single-use, disposable auto-injector have entered the market in other therapy areas. These have, to date, been in high-value markets where the additional cost of a disposable device is easily justified by the benefits it offers. These devices generally contain a single dose in a pre-filled syringe. In their design, industrial and human factors have been carefully considered to address the needs of patients who are self-administering injections. As the patient does not have to prime, load or unload the device, there are clear safety and usability advantages over re-usable devices. As well as the benefits for patients, the single-use disposable format offers both opportunities and challenges to medical device manufacturers and pharmaceutical companies.

For the medical device manufacturer, the fact that a disposable device need only function once allows device designers to produce an impressive range of features that it would be difficult to achieve in a re-usable device. These often include passive, integral safety features to prevent accidental actuation and minimise the risk of needlestick injuries occurring before and after the injection. Engineering feature-rich designs brings with it complexity and the associated challenges of producing a reliable product in high volumes. Owen Mumford Ltd, a UK-based manufacturer of auto-injectors, comments that: ‘To support the increased output requirements for our disposable business, we are seeing investment in higher cavity tooling and automated assembly machinery as well as investment in new facilities to provide the increased manufacturing space required. This is certainly a very exciting time for the auto-injector market’.

In the past five years, there has been a great deal of activity in the field resulting in a large number of patents. The intellectual property gold-rush may well be nearing its conclusion — but only a few designs have made it to market to date and so it is likely that a number of similar, competitive devices will be launched within the next two to three years. Also, some early examples of auto-injector design will be coming off patent soon, and so it is possible that these may be manufactured as generic devices, driving device companies to compete on cost. This may serve as an enabler for auto-injectors to become economically viable in lower-value therapy areas.

Compromises in Device Design

A feature common to many of the current, commercially-available auto-injectors is that they are engineered around a standard pre-filled syringe for manual injection. This feature is predominantly driven by pharmaceutical companies making an early commitment to a primary packaging format during formulation development, or when re-formulating an existing product in a liquid-stable form. Pre-filled syringes are a mature technology and represent a low-risk option for achieving and demonstrating formulation stability. A standard format also offers flexibility in the supply chain as pharmaceutical manufacturers can use a number of contract filling suppliers to cover multiple geographies. However, engineering an auto-injector around a pre-filled syringe designed for manual injection necessitates compromises in the design. The alternative solution is to design a custom primary pack format specifically for use with an auto-injector. This may not be economically viable for a medical device manufacturer to undertake for a single product line, but it seems likely that growth in demand for such a cartridge may reach a level where it becomes a compelling proposition for a syringe system manufacturer to produce a primary packaging format which is optimised as a platform for developing auto-injectors.

FUTURE OPPORTUNITIES

Innovative medical device companies will continue to enhance the benefits offered by auto-injectors. As the
new generation of single-use disposable auto-injectors matures in the market, user feedback will ensure that designs evolve and improve. It is difficult to predict what direction these developments will take, but they may include the following.

**Greater Control for Patients**

One commonly reported observation from patient groups is that they like to feel that they are able to control the rate at which the injection is administered. Having more control over the process may give the user physical and mental advantages in the control of pain and anxiety.

**Smart Packaging**

Packaging designers have long since realised that packaging can be more than just a protective shield. Packaging innovations – such as temperature monitoring strips – can add functional features to improve safety or guide the user as they engage with and dispose of the auto-injector (see Figure 4).

**EXTENSION TO NEW AREAS**

With the benefits of auto-injectors widely acknowledged, it seems likely that their use will extend into new areas.

**Reconstitution of Lyophilised Drug Products**

Drug products that are not stable in solution are often lyophilised in standard glass vials. The reconstitution and delivery of these compounds is considerably more complex than an injection from a pre-filled syringe and may not be achievable for some users. Proprietary designs of dual chamber cartridges, which do an excellent job of simplifying the whole process, have been available for several years now, but have so far found few applications. This is probably due to a combination of the increased cost and perceived risk of employing a non-standard primary packaging format. It is likely that medical device manufacturers will produce designs that simplify the process whilst still using a standard vial and lyophilisation process, thereby achieving a balance between user requirements and the technical and commercial risk borne by the pharmaceutical company. This has the potential to open up opportunities for self-administration of many existing and future drug products.

**Intramuscular Delivery**

Drugs administered by intramuscular injection will bring fresh challenges for device designers, including the potential need to expel any air that is present in the primary package and avoiding delivery into major blood vessels.

**CONCLUSION**

Automatic injection devices offer wide-ranging benefits to both users and businesses. Growing concern over the hazards associated with needlestick injuries and a realisation of the benefits offered by drug delivery devices has stimulated a period of rapid growth in the market for single-use, disposable auto-injectors. This been accompanied by a resurgence in the market for re-usable devices. It is likely that the next few years will see the variety of auto-injectors on the market continue to grow, with competition to meet requirements spurring innovation in new therapy areas. The deserved success of these devices is underpinned by the principles of quality, safety and efficacy, and will certainly continue to be an important part of patients’ lives – particularly those who enjoy the benefits of taking an active role in their treatment.

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**References**