THE RISE OF LARGE-VOLUME INJECTORS IN A PATIENT-CENTRIC ERA

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DATWYLER

INTRODUCTION: THE GLOBAL TREND TOWARDS SUBCUTANEOUS BIOLOGICS

Advances in drug delivery are enabling patient-centric, home-based care, with a key driver being the rise of large-volume injectors. These are devices that can administer high-dose or high-viscosity biologic drugs subcutaneously instead of intravenously. Before trastuzumab's 2013 launch, the maximum recommended subcutaneous injection volume was 2 mL. This increased to 5 mL at that time, and now volumes up to 20 mL can be delivered subcutaneously.

Traditionally, many monoclonal antibodies and oncologics required intravenous (IV) infusions in clinical settings, but reformulated subcutaneous (SC) versions delivered via auto-injectors or on-body delivery systems (OBDS) can achieve comparable outcomes within minutes of injection time. For example, the cancer therapy daratumumab was converted from a three to seven-hour IV infusion to a five-minute SC injection, and today, more than 90% of US patients receive the convenient SC form.

In this report, we examine the accelerating global trend toward large-volume injectors, from handheld auto-injectors to advanced wearable devices, exploring how these delivery devices in combination with new formulation technologies are reshaping the administration of complex biologics, including oncologics and chronic disease therapies.

SAFETY AND QUALITY OF LIFE: EVOLUTION IN INJECTOR DESIGN

While early auto-injectors such as the EpiPen were developed for emergencies and military use, delivering small volumes intramuscularly in one quick shot, their use has since expanded to routine therapies.

Modern auto-injectors have been re-engineered to accommodate biologics. Unlike manual injection, an auto-injector's spring mechanism can deliver a dose with controlled force and speed, which is important for fragile biologics. Auto-injectors also generate higher force than a person could, making it feasible to push high-viscosity formulations through a fine needle. Another advantage of auto-injectors is their integration of automatic needle insertion and retraction mechanisms. Once an injection is complete, the needle retracts safely inside the device, eliminating accidental needle-stick injuries to patients or healthcare staff.

Auto-injectors can be either prefilled syringe (PFS)-based or cartridge-based. Cartridge-based systems insert the needle at the moment of use, while in the case of PFS-based auto-injectors, the needle is already in place from the moment of filling. When the drug shows the tendency to clog in the needle during storage, cartridge-based systems might offer a better solution.

Standard units historically held ~1 mL, followed by 2.25 mL models for drugs such as hormonal treatments and some antibodies. Today, novel auto-injector models are stretching the limit to 5 mL in a single delivery. This has created opportunities for many monoclonal antibody therapies to be packaged in auto-injectors, improving patient convenience.

Introducing on-body injectors

At the centre of patient-centric care are wearable medical devices. Also known as on-body delivery systems (OBDS), wearable injectors are systems including a controlled dose delivery mechanism that a patient adheres to the body and can leave in place while the drug infuses over an extended period. Because the patient isn't actively holding it, injection can safely take much longer, enabling much larger volumes to be administered comfortably.

Wearables are more complex, with most using electromechanical drives rather than simple springs, and often include electronics for timing and feedback. To keep costs reasonable, some wearable designs split the device into a reusable main unit and a disposable drug cartridge module. In such cases, only the lower-cost module, containing the drug reservoir, cannula, and adhesive, is thrown away after each dose, while the core unit is reused for multiple treatments, supporting a more sustainable model. Advanced adhesives keep devices secure during lengthy infusions but allow easy removal without harming skin.

Wearable injectors deserve special focus as they are a linchpin for delivering the largest volumes outside of clinical settings, and they are making an impact in fields such as oncology, immunology, and blood disorders. A prominent use-case is post-chemotherapy supportive care. Traditionally, patients receiving chemo might return to the hospital the next day for an injection of growth factors, but now, an on-body injector can be applied during the chemo visit and programmed to automatically inject the drug 27 hours later, sparing the patient an extra trip to the clinic.

On-body systems typically deliver volumes between 5 and 20 mL. Once above 20 mL, pump systems can be used to administer medicines in a home care setting, though these are not attached to the body.

Overall, while wearable systems have the advantage of home care administration, they offer longer injection times and reduced convenience when compared to auto-injectors. Therefore, new drugs are typically brought to market in an auto-injector rather than an OBDS whenever possible.

Supporting patients

For patients, the shift from clinic-administered IV infusions to home self-injection reduces or eliminates the hospital visits that disrupt daily life and work. In many cases, treatments that were once daily injections can be given in weekly or monthly doses thanks to the large-volume and long-acting nature of SC formulations. Fewer injections mean less burden on patients and potentially better medication adherence.

However, there are also many challenges linked to this shift from hospital care to home care. Patients must have the confidence and the ability to inject themselves.

Therefore, auto-injectors and wearables are designed to be as simple as possible to operate, even for those with limited dexterity or needle phobia. Spring-driven auto-injectors conceal the needle and control the injection speed, so the patient does not have to precisely push the plunger. This can reduce injection anxiety and ensure the medication is delivered at the proper depth and rate every time.

Devices also often incorporate ergonomic grips and low activation force, catering to elderly or arthritic patients. Furthermore, by automating the process, these injectors remove user error, as the correct dose is pre-measured in a cartridge or syringe, and the needle insertion and retraction are automatic.

To promote drug safety and effective side effect management in home care settings, digital device connectivity is used. Devices can be equipped with advanced monitoring features that transmit dosing information and patient-reported outcomes to healthcare teams. This enables the early identification of adverse events and facilitates timely interventions, even in the absence of on-site healthcare providers.

TECHNOLOGICAL ENABLERS: ADVANCEMENTS IN LARGE-VOLUME INJECTABLES

Several technological breakthroughs are driving the successful rise of large-volume injectors, encompassing novel approaches to SC formulation science and innovations in container materials and needle design.

SC formulations

One key innovation has been permeation enhancer technology, notably Halozyme's ENHANZE platform, which utilises recombinant human hyaluronidase. Hyaluronidase temporarily degrades hyaluronan in subcutaneous tissue, significantly increasing the space for fluid to disperse. This allows injection of larger volumes into the SC layer that would otherwise be very difficult due to pressure build-up. The enzyme is co-formulated with the drug and, once injected, it creates a broader diffusion area in the tissue. Together with advanced devices, these formulation innovations allow the transition from an IV drug to a subcutaneous drug by overcoming natural physiologic limits. This means that several cancer drugs that were IV-only have been reformulated with Halozyme's enzyme so they can be given subcutaneously in one large injection. Further, dozens of approved or pipeline biologics now leverage hyaluronidase to enable SC doses of molecules such as monoclonal antibodies that would have previously required IV infusions.

Another approach is developing concentrated biologics for subcutaneous delivery. Elektrofi's Hypercon platform uses microparticle suspension technology to create stable, highly concentrated formulations—up to five times stronger than standard versions—for easier subcutaneous administration. This technology offers a formulation stable at room temperature and reduces the number of injections required. However, its use of a non-aqueous carrier introduces added complexity for compatible rubber materials used within primary packaging.

Drug container innovation

The development of polymer drug containers, such as cyclic olefin polymers (COP/COC), offers options besides glass. Polymer containers allow for more sophisticated and complex device designs, which is crucial for drug delivery systems and miniaturisation, an advantage that glass cannot match. They are also lighter in weight and much less brittle than glass, significantly reducing the risk of breakage during handling and use.

Needle innovation

Recent developments in ultra-thin-wall needles have made it possible for higher flow rates by thinning the needle walls and expanding the inner lumen—without increasing the needle's outer diameter. The force needed to inject is directly related to the length of the needle and inversely proportional to the fourth power of its radius. For example, an 8 mm, 27G Special Thin-Wall needle features a larger internal diameter, which lowers hydrodynamic resistance. As a result, injections become easier and less painful for patients, allowing even thick biologic medications to be delivered comfortably with minimal effort.

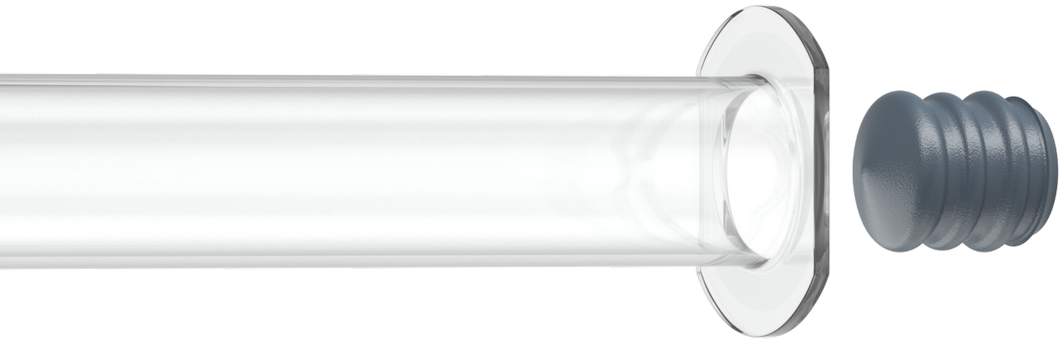
MARKET DYNAMICS: THE OUTLOOK FOR LARGE-VOLUME INJECTORS

In the pharmaceutical pipeline, 15% of all biopharmaceuticals in development or on the market could be classified as large-volume SC candidates (doses over 2 mL). This includes at least 182 products, predominantly monoclonal antibodies and other complex biologics, targeting diseases from cancer to autoimmune and cardiovascular conditions. Notably, many of the oncology biologics are still given by IV and represent a significant opportunity for SC conversion, whereas the majority of non-cancer biologics in this category are already being developed for SC use.

Regulatory agencies have also paved the way by creating pathways for combination product approval and encouraging innovation in drug delivery for patient benefit. The US Food and Drug Administration (FDA) has approved several on-body injector systems as part of combination products, establishing precedents and guidelines for safety and efficacy evaluation. Approved in December 2023, one example is UDENYCA ONBODY™, a wearable presentation of UDENYCA®, a pegfilgrastim biosimilar. UDENYCA ONBODY offers several advantages over the OBDS reference product, the Neulasta® Onpro®. These include a reduced injection time of five minutes rather than 45 minutes, improved adhesion, and automatic needle retraction. With such improvements resulting in increased customer convenience, UDENYCA had a market share of 41% by the end of 2024. This example highlights the importance of differentiation when launching biosimilars and the role of packaging systems in achieving this.

In Europe, the European Medicines Agency (EMA) guidance highlights device usability, materials compatibility, and risk management, requiring robust evidence that device components will not compromise drug stability or patient safety. Other regions are also moving in this direction, including Japan's PMDA which has expanded its requirements for device–drug combinations, while regulatory agencies in China and India are beginning to issue guidance on connected injectors and reusable platforms. As large-volume devices become global standards of care, harmonisation of testing protocols, from leachables and extractables to mechanical reliability, will be essential.

Established medical technology companies and startups alike are vying to provide the next successful injector platform. Some large device manufacturers have opened new production facilities dedicated to auto-injectors, anticipating rising demand. Contract manufacturers are also scaling up capabilities for assembling injectors and combination products. Simultaneously, pharma–device collaborations are on the rise, with pharmaceutical companies partnering with device specialists early in development to tailor delivery devices for their specific biologic.



THE ROLE OF ELASTOMERS: EXPLORING DATWYLER'S NEOFLEX™ PLUNGERS

As the industry embraces large-volume injectables, component suppliers such as Datwyler play a crucial role in making these delivery systems possible. Driven by values such as entrepreneurship and the desire to exceed quality standards and customer expectations, Datwyler is a leader of innovation when it comes to elastomeric components for parenteral packaging. The company's latest contribution is the expansion of its NeoFlex line of coated plungers – an innovative example of the material advancements needed for large-volume, sensitive biologic formulations.

In any pre-filled syringe or cartridge, whether in an auto-injector or a wearable device, the rubber plunger and stopper are in direct contact with the drug. For biologics, this contact must be as inert and clean as possible. NeoFlex plungers are precisely engineered to reduce particulate contamination, vital for injectable drugs where even slight contamination risks recalls or regulatory issues. Fully coated, they prevent rubber shedding, while their natural lubricity removes the need for silicone, ensuring smooth, reliable performance while upholding strict cleanliness standards.

NeoFlex plungers ensure reliable container closure integrity even in challenging conditions like transport or extreme temperatures. With smooth, consistent gliding, they seamlessly fit all siliconised barrels and drug delivery devices, delivering precise, effortless injections every time. Datwyler's NeoFlex also embodies sustainability, boasting a lower carbon footprint than other coated solutions. Its non-fluorosurfactant fluoropolymer ensures safety for both people and the environment. Furthermore, advanced camera inspection guarantees exceptional standards, minimising waste and reinforcing environmental responsibility.

NeoFlex plungers are now engineered for large formats, with Datwyler developing versions to fit into syringes and cartridges up to 20 mL commonly used as containers for auto-injectors and wearable devices. For cartridges, Datwyler provides a complete solution: a cartridge plunger plus a matching 13 mm serum stopper or DuraCoatTM combiseal for the front end, with both components made with the same contact material. This reduces the complexity of the system's E&L profile, allowing pharma companies to confidently fill high-volume cartridges for on-body injectors by mitigating the risks associated to the drug quality over its shelf-life and during the stress of delivery.

Another advantage of the fully coated NeoFlex plungers is their compatibility with oily suspensions. Such suspensions have posed complexities for rubber materials which swell when in contact with them, affecting the component's functionality. Fully coated rubber components avoid this swelling. The complete coating around the plunger ensures that there is no risk of contact between the rubber and the drug product, something which cannot always be guaranteed with partially coated solutions on the market.

Meanwhile, Datwyler has expanded its FirstLine® production capacity across Europe, Asia, and a new US facility to supply these plungers in the huge volumes that blockbuster biologics will require. The company has invested in flexible production lines where the same equipment can switch between different product types as demand shifts, such as OmniFlex® coated vial stoppers and NeoFlex plungers, ensuring high responsiveness to market needs. This flexibility and global footprint mean that as therapies related to sensitive biologics and next-generation antibodies surge in demand, Datwyler can ramp up component supply without bottlenecks.

Additionally, by being available in a sterile, ready-to-use format using steam or gamma, NeoFlex plungers support high-speed aseptic filling processes and can integrate into existing pharmaceutical manufacturing with minimal changes.

By solving the material challenges, such as preventing biologic degradation, minimising particulates, and overcoming the issue of scale, NeoFlex facilitates the industry's move toward patient-friendly injections.

Conclusion

The global shift toward large-volume injectors is driven by the growing demand to deliver modern biologic therapies in ways that are patient-centric: convenient, safe, and effective.

Looking ahead, the landscape for large-volume injectables is dynamic. As more biologic drugs come to market, especially for chronic diseases and oncology, the demand for advanced delivery solutions will continue to grow. We can expect continued refinement in device design, investment in making devices more intuitive and integrative, and a continued focus on sustainability. Meanwhile, the role of component suppliers such as Datwyler will remain critical in innovating the materials and components that ensure these devices work seamlessly with delicate biologic drugs.

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