Robust by design – how BD is overcoming the biologics challenge in drug delivery

BECTON, DICKINSON and Company (BD) is developing a 2.25mL dose volume fully integrated autoinjector with BD Neopak™ XtraFlow™ - BD's latest pre-fillable glass-based syringe system featuring an 8mm needle with ultra-thin wall cannula technology.

BD has designed autoinjectors that can deliver drugs of differing viscosities in a well-integrated robust system. Pharmaceutical companies can adapt BD Intevia™ to deliver a range of drug volumes and viscosities without any need for customisation of the system or its components.

BD recently launched BD Intevia™ 1mL, capable of managing viscosity up to 35cP, and is currently developing a 2.25mL version, with the ability to handle viscosity up to 40cP. BD Intevia™ 2.25mL is designed as a patient-centric device, reliably integrated with BD Neopak™ XtraFlow™ pre-fillable syringes, offering a shorter needle (8mm) with ultra-thin wall (UTW) needle technology. This XtraFlow™ technology increases the inner diameter of the needle by reducing the thickness of the needle wall, without expanding the external diameter. The aim is to enhance user injection experience and comfort while delivering viscous drugs.[1]

Both BD Intevia™ 1mL and 2.25mL platforms offer the potential for significant cost savings for pharmaceutical manufacturers because major de-risking development process activities, such as pre-clinical, clinical and human factor studies, have been conducted to confirm device maturity.[2] Device manufacturers need to ensure a high compatibility between biotech drug, primary container and secondary packaging.[3] The objective is to minimise and prevent issues that pharmaceutical companies could encounter during combination product development stages that might affect time-to-market and associated costs.[2]

Biologic therapies have revolutionised the treatment of chronic diseases, but their viscosity, volume and injectable formulation can present challenges. The BD cross-functional development team has designed a robust system solution, leveraging its experience and the lessons learnt after 10 years of market commercialisation of the BD Physioject™ autoinjector integrated with a BD pre-fillable syringe.[4,5]

System delivery challenges arise when device components are obtained from separate sources, as they must operate in conjunction once assembled.

BD's robust engineering process had to enable the primary container and BD Intevia™ autoinjector to work together effectively as one integrated system. To help achieve this, we first defined the requirements of the delivery system, the subsystems and the components within, as well as all the manufacturing processes involved.

Self-injection using primary or secondary devices enables patients to take control of their treatment journey and BD is dedicated to deliver best-in-class product performance and services by applying the latest advances in drug delivery technology.

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European Pharmaceutical Review – BD Intevia™ 2.25mL White Paper

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BD is developing a 2.25 mL dose volume fully integrated autoinjector with BD Neopak™ XtraFlow™ - BD's latest pre-fillable glass-based syringe technology featuring an 8 mm needle with ultra-thin wall cannula technology. The BD Intevia™ autoinjector has recently received the Frost & Sullivan Global 2020 Technology Innovation Award in the autoinjector drug delivery device category. Frost & Sullivan's Best Practices Awards recognise accomplishments in innovation and disruptive technologies.

BD designed autoinjectors that can deliver drugs of differing viscosities in a well-integrated robust system. Pharmaceutical companies can adapt BD Intevia™ to deliver a range of drug volumes and viscosities without any need for customization of the system itself or of its components. BD recently launched BD Intevia™ 1 mL, capable of managing viscosity up to 35cP, and is currently developing a 2.25 mL version, capable of managing viscosity up to 40cP. BD Intevia™ 2.25 mL is designed as a patient-centric device, reliably integrated with BD Neopak™ XtraFlow™ prefillable syringes which offers a shorter needle (8 mm) with ultra-thin wall (UTW) needle technology. This XtraFlow™ technology increases the inner diameter of the needle by reducing the thickness of the needle wall without having to increase the external diameter with the aim of enhancing user injection experience and comfort while delivering viscous drugs.[1]

Both BD Intevia 1 mL and 2.25 mL platforms offer potential for significant cost savings for pharmaceutical manufacturers because major de-risking development process activities such as pre-clinical, clinical and human factor studies are conducted to confirm device maturity.[2] Device manufacturers need to ensure a high compatibility between biotech drug, primary container, and secondary packaging.[3] The objective is to minimise and prevent issues that pharmaceutical companies could encounter during combination product development stages which might affect time to market and development costs.[2]

Lionel Maritan, Research and Development Associate Director at BD who is responsible for Design, Development, and Life Cycle Management activities for Autoinjectors and Safety Solutions, and Karima Yadi, Global Marketing Lead for the autoinjector platform at "BD Medical Pharmaceutical Systems", discuss the innovation behind BD Intevia™ 2.25 mL.

Chronic disease market

Biologic therapies have revolutionised the treatment of chronic diseases. Their development was supported by significant innovations in formulation development and injection devices, resulting in 80% of biologics now being delivered by subcutaneous self-injection which can be performed at home rather than by intravenous infusions in clinical settings.[4]

The ability to deliver biologics via subcutaneous injection has transformed patient management of a wide range of conditions including rheumatoid and psoriatic arthritis, diabetes, multiple sclerosis, Crohn's disease, and other autoimmune, metabolic, and chronic inflammatory disorders.

Today, more than 70 million Americans aged 50 and older – four out of five older adults – suffer from at least one chronic condition, while 11 million of those live with five or more chronic conditions.[5] As the population ages, the prevalence of chronic diseases will increase. According to the World Health Organization, chronic diseases are by far the leading cause of mortality in Europe,

representing 77% of the total disease burden and 86% of all deaths.[6] Without effective medical interventions, these conditions can be life-limiting and pose a significant burden for healthcare systems.

People living with chronic diseases such as rheumatoid arthritis and diabetes have previously dealt with restrictive treatment regimens, involving frequent visits to primary care units.[7] For most biologics, intravenous infusions are the conventional drug delivery method and this administration allows for significantly higher drug administration volumes.[8] In general, we can say that a higher proportion of the administration costs of biologic drugs given subcutaneously or intramuscularly come from the proximal cost incurred before or after drug administration while for intravenous products, costs are incurred in both cost centres.[9]

The subcutaneous drug delivery route has offered patients greater flexibility with home injections and provided considerable savings for healthcare systems.[9] Autoinjectors used with pre-fillable syringes offer multiple benefits, from providing an accurate dosage to the reduction of needlestick injuries as needles are protected after use.

Advances in the concentration of biologics

Biologics are the fastest-growing pharmaceutical sector and led the top selling drugs in 2017.[10] In 2018, the biologics market was valued at 251.5 billion USD and is predicted to grow at a compound annual growth rate of 11.9%, with forecasts for 2026 eclipsing 625.6 billion USD.[11] In 2019, 40% of the over 16,000 drugs in the global pharmaceutical pipeline are biologic therapies.[12] Biologics are far more complicated at the molecular level than traditional chemically synthesized pharmaceuticals. The molecular structure, size, manufacturing, and administration of these therapies all contribute to their complexity.[13]

The viscosity, volume and injectable formulation of biologics can represent development challenges of drug-device combination products, as well as challenges from a user's perspective.[14] It is important to take these factors into consideration when designing an injectable drug delivery solution to ensure a patient-friendly and robustly-performing device.

Effective use of medicines is an important part of self-management of chronic conditions. However, many patients do not take their medicines as intended by the prescriber. According to the European Patients Forum, it is estimated that 50% of chronic disease patients may not follow their long-term treatment regimens.[15] Issues like injection site discomfort, frequency of injections and self-injection fears have negatively impacted the patient experience.[16] In addition, patient empowerment[17] and low confidence or engagement levels have been cited as issues that can impact medication adherence.[18] To combat these challenges, patient feedback has been used to develop a range of self-injection devices. Providing different devices for drug administration can give patients the opportunity to choose a device that meets their specific needs and addresses the challenges they face as an individual.[19]

BD's cross-functional development team have designed a drug delivery solution to fit not only for the biologics currently available, but also those in development. To meet unmet needs around the challenges of administering biologic drugs[20] and enhancing patient injection experience, the BD cross-functional development team has designed a robustly designed system solution, leveraging its long experience and the lessons learnt after 10 years of market commercialisation of the BD Physioject™ autoinjector integrated with a BD pre-fillable syringe.[21,22]

Integrated systems solutions

BD has a long-term commitment to creating robust self-injection solutions that leverage its state-of-the-art primary containers and needle technology and pre-fillable drug delivery systems expertise. With insights from previous products, the cross-functional development-team identified a clear need for a high-quality, fully integrated system that would deliver the drug to patients in an effective way with reproducible performance across millions of units.

The parameters that help build a robust drug delivery system include rigorous human factors studies such as usability and ergonomy. To de-risk the development process to deliver high viscous drugs and high volume subcutaneously, pre-clinical and clinical studies can help measure the reliable injection depth and pain perceptions levels. Needle length and inner diameter are also key parameters of consideration as these latter will impact the flow, the injection force and time of injection.

The creation of a drug-device combination can be a long and expensive process. System delivery challenges arise when device components are obtained from separate sources, as they must operate operatively in conjunction once assembled. A poor fit can lead to device failure or inconsistent injection times. Such complex systems increase the number of functional interfaces and thus introduce several challenges such as an increase in total injection time, patient discomfort, and issues with mechanical injection force.[23]

To eliminate the risks associated with integration of components from diverse manufacturers and those associated with the customization of the secondary device, the engineering process should be mastered to bring the primary container and the secondary device co-operating together in one performing system. A robust set of data demonstrating this performance should be generated. BD is able to manage this engineering process during the definition and development phases of the container and device. Typically, a series of cascading requirements will be defined: defining the delivery system requirements leads to defining those of the subsystems, then those of each component and eventually those of the manufacturing processes involved. Moreover, the company's capabilities cover all design control aspects, including usability (human factors) engineering, and preclinical and clinical evaluation.[1,24]

Pain perception, injection-related anxiety and IM injection risks

A key factor in the BD Intevia™ design will be addressing the issue of pain experienced by chronic disease patients and injection related anxiety.[14] The high viscosity and volume of biologics places mechanical force and back pressure on devices.[23] BD's engineers sought to design a device that could deliver the correct dose of high viscous biologic therapy within 10 and 15 seconds for the 1 mL and 2.25 mL volume respectively. This can be achieved with the integrated autoinjector technology approach to manage the variance and variability of all component interfaces for robust subsystem integration and compatibility.

BD Intevia™ 2.25 mL device utilises BD's latest innovation in needle technology – the BD Neopak XtraFlow™ pre-fillable glass-based syringe solution featuring an 8 mm needle with thinner wall cannula technology. This smaller needle size, compared with a standard 12.7 mm needle, can help to reduce pain perception, injection-related anxiety, and intramuscular injection risks.[25 26]

Patient-centric product development

BD has generated robust data to showcase the high performance of BD Intevia™, incorporating all design aspects from the patient perspective on usability and product engineering to preclinical data.

Our human factors engineering identified device failure incidents and sought solutions. These insights enabled the BD team to design an autoinjector that delivers the appropriate medication dose of a high-volume biologic. BD can provide advanced data on stack up tolerances, across a broad portfolio of BD specialised systems, to help pharmaceutical companies anticipate system performance.

A patient-centred approach was integral to BD's Intevia™ design. Many people living with chronic disease who manage their disease with biologic treatments often need to routinely use injectable therapy. They need a simple but reliable system. To use the BD Intevia™ device, a patient simply places it against their skin and pushes the needle cover against the skin to deliver the prescribed dose. Patients also require reassurance of the delivery of the dose. BD Intevia™ offers this two-fold, with a visible indicator that confirms the prescribed drug dose has been delivered and an audible 'click' sound.

Summary

BD's insights on product development and evidence of our system performance help to ensure that pharmaceutical drugs get delivered as intended to patients. BD's robust engineering process had to enable the primary container and BD Intevia™ autoinjector to work together effectively as one integrated system. To help achieve this, we had to first define the requirements of the delivery system: the subsystems, and the components within them and then all the manufacturing processes involved.

A well-integrated autoinjector system can provide significant cost savings for pharmaceutical companies and their partners in the long-run. It is paramount that new device designs minimise the costly issues that pharmaceutical companies often encounter during combination product development stages.

Self-injection using primary or secondary devices enable patients to take control of their treatment journey, and BD is dedicated to deliver best-in-class product performance and services by applying the latest advances in drug delivery technology.

About the authors

Lionel Maritan joined BD in 2005 and has deep experience in Drug Delivery Systems Design and Development from the innovation stage to commercialisation. He has a MSc in Engineering with a specialization in plastic parts design and manufacturing.

Karima Yadi provides commercial leadership to BD's delivery system platforms and defines, develops, and launches patient-centred injection solutions in collaboration with cross functional, commercial, and regional teams. She has a BSc (Hons) in Management Science from University of Warwick Business School, and an MSc in International Business Management from London South Bank University.

About BD

BD – Becton, Dickinson and Company - is a global, industry-leading medical devices manufacturer, proving drug delivery systems for 70% of the top 100 pharmaceutical companies.[27]

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