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Biologic Medicines and Patient-centricity – A New Phase of Hope

The global pharmaceutical industry has entered an exciting new era of drug development, bringing new hope to patients around the world. It is estimated that close to 40 per cent of all medicines in pipeline development are biologic in nature.

The world's top-selling commercial biologic medicines cover a broad range of diseases – including autoimmune challenges such as various forms of arthritis and psoriasis, Crohn's disease, ankylosing spondylitis, ulcerative colitis, as well as other conditions such as multiple sclerosis and macular degeneration – bringing hope to many long-suffering patients.

Biologic medicines have also transformed treatment and personal care for a significant portion of the diabetes patient population. Furthermore, biologics have provided breakthrough therapies in the advanced treatment for various forms of cancer, where more than 70 new therapies have entered the market within the past five years, many of which are biologic in nature.

Within the last few years, favourable incentives have also encouraged the use of biologics to treat rare and orphan diseases, bringing much-needed hope to a significantly under-served population. In the US, the FDA has approved record numbers of new drug approvals in the consecutive years 2016 and 2017, as well as keeping pace in the first half of 2018. Drugs with special designation including orphan, breakthrough, etc. have comprised approximately 40 per cent of new FDA drug approvals over this 30-month period[1]. It is also noteworthy that approximately 25 per cent of these new drugs represent cancer therapies[1].

It is also worth noting that biologics represent big business potential for drug developers. The top ten biologic medicines comprise therapies with annual global revenues in excess of $71 billion[2]. Biologics represent seven out of the top ten best-selling medicines across all therapeutic categories[3]. There are currently more than 45 biologic medicines on the market that have reached blockbuster status (selling more than $1bn annually) and ten biologic medicines yield sales in excess of $5bn globally. The total biologic market is expected to reach $390bn by 2020[4].

The rise of biosimilars, or generic biologics, represents another attractive growth opportunity for the pharmaceutical industry – and is a perceived win for the patient population by way of reduced access and decreased cost through market competition. Biologic medicines facing patent expiration represent noteworthy biosimilar market opportunity for a multitude of developers. By 2020, biosimilars have the potential to enter the market for brand biologics currently representing more than $45bn in global sales[4].

Changes in Drug Delivery Bring New Freedoms

The advent of biologic medicines brings considerably different forms of drug delivery compared to traditional oral solid-dose medications. In the early days of introducing biologic medicines to the healthcare market, drug products were commonly delivered in traditional glass vials requiring ancillary components for administration – such as syringes or needles of various gauges depending on drug and patient tolerance, potentially paired with safety applicators or other devices. These medicines may have been self-administered by appropriately trained patients, but more commonly they were administered by healthcare professionals in clinical settings. The implications of this method of delivery require frequent visits to healthcare facilities by patients to seek treatment, which – for some diseases – could be multiple times per week. This continues to be a common platform for many institutionally administered medications.

With the progressively competitive landscape and the healthcare industry's initiative to become more customer-focused, or 'patient-centric' – coupled with the payer community's desire to limit patients being onsite in clinical settings to reduce the cost burden – more focus and resource has been placed on advancing drug delivery forms to allow easier routes of administration for patients. In some instances, this is driving development of better methodologies for drug delivery in the clinical setting, but increasingly the focus has been to provide safe, reliable and convenient forms of drug delivery for patients to self-administer, with the goal of minimising the impact to their everyday lifestyle and providing more freedom from the burden of receiving their medication in a formal healthcare setting.

Diabetes care is one great demonstration of the popularity of this developing technology, with multi-use – and often refillable – injectible insulin pens spreading past developed markets in North America and Europe, rapidly progressing now into developing and third world countries.

This transition has generated new paradigms for patients, providing more freedoms but also shifting the burden of responsibility for safe and accurate dosing from the clinical environment to the patient. This raises the stakes considerably for the pharmaceutical company, which needs to ensure that the patient is best positioned for success. In fact, even the best and most effective medication would fail to garner FDA approval without the execution

and successful demonstration of comprehensive human factor study analysis; that this has been performed and has shown that the average patient can administer the therapy easily, effectively, and repeatably.

The Impact of the Transition for Injectibles

The popularity of prefilled syringes has grown considerably over the past few decades; the current global market is estimated to be between three and four billion syringes annually, with projected growth of between eight to ten per cent, year-on-year, fuelled largely by the burgeoning Asian market[5].

The familiarity and growth in the diabetes market has provided significant economies of scale in the syringe market, as well as provided the platform for advancing syringe material and delivery technologies. As the market has progressed to consideration of safety and ease of use, exciting new developments have been introduced to both aid the injection process for patients, and to provide safety measures to reduce potential for accidental needle sticks or other concerns. Innovative approaches have been taken to engineer solutions for sheathing needles with protective covers, triggered by use, or retracting needles into the housing of the prefilled syringe system. Likewise, patient comfort has been better addressed in advanced delivery systems with refined needle technologies, particularly impactful for large-volume injections.

Such advanced prefilled syringe delivery and added safety features bring increased complexity in assembly and handling. Precise multi-part integrated assemblies with precision-moulded plastics and spring-based systems demand expert automated solutions, complete with multi-stage in-process inspection to ensure the accuracy of each sequential assembly. This systematic and sequential approach to assembly provides consistency in mitigating risk and maximising safety, ensuring reliable delivery in every dose. Failure in accuracy for any individual assembly would likely result in a failure of the intended feature. PCI's investments in cutting-edge technologies have focused on robust multi-level inspections to ensure that safety and accuracy are consistently and reliably achieved for these complex assemblies.

Pens and Autoinjectors – the Next Generation of Convenience

The success of products such as Enbrel, Avonex and Lantus has paved the path for the advancement of autoinjector and pen technologies, rapidly progressing this as an important growth category for the biotech market. The sheer scale of the market has made investment attractive for the category.

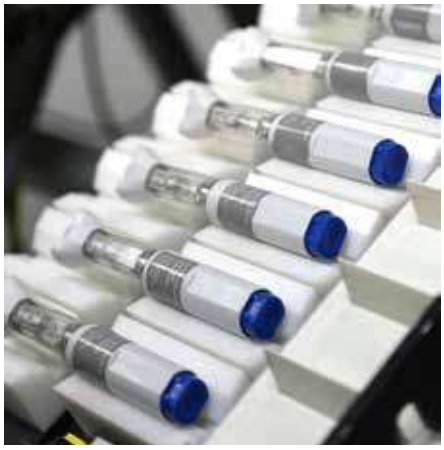
Whereas initial pioneers in the autoinjector and pen markets were once forced to create and engineer their own technologies, leading providers – such as Ypsomed, SHL Group, Beckton Dickinson, West and others – have now created portfolios of 'off the shelf' proprietary innovative delivery systems built on standardised syringe or cartridge deliveries from sterile manufacturers. These solutions provide standardised volumetric-based platforms, taking into account other critical factors such as product viscosity. Advancing medicines are pushing the envelope for longer-lasting medicines; reducing frequency of injection, but often requiring larger volumes of liquid-based delivery. This has pushed the industry to develop larger-volume injection systems, sometimes pushing wearables as a more optimal solution when autoinjectors may not be conducive to the duration of administration for patients.

Neulasta's new wearable delivery is a great example of how this can transform patient care and truly deliver freedom for patients. Innovative dual-chamber technologies also provide for simple reconstitution for marrying lyophilised drug products with sterile water for injection, simplifying preparation and administration of these drug forms – further providing freedoms for patients looking to self-administer and minimise trips to the clinic.

Injectible Devices and Tertiary Packaging for Delivery – a Comprehensive Approach

With the market developing and furthering exciting new delivery technologies, consideration must also be made in packaging forms to deliver the drug device to the end user. The push towards patient-centric solutions and enabling freedom from the healthcare setting for product administration creates a dynamic where it is vitally important that pharmaceutical companies put considerable thought and preparation into the packaging by which the device is delivered. Furthermore, the premium nature of the medication warrants careful consideration to ensure successful navigation of the supply chain, as well as providing a user experience consistent with their expectations for a premium product.

Secondary packaging plays a vital role in ensuring the product navigates the complex supply chain safely and securely, and in the considerations for end delivery to the patient. Product protection is paramount. Sophisticated drug delivery devices are often designed around combinations of glass, plastic and other elastopolymers that are susceptible to breakage if mishandled. Furthermore, the complexity of these advanced drug delivery systems demands appropriate protections from the elemental forces of shock and vibration in the distribution system, coupled – and sometimes exacerbated by – refrigerated or frozen conditions in the required cold chain environment. Protective packaging must be both useful in its intended form, as well as elegant and sophisticated, marrying the advanced device with its other critical components in a cohesive and functional system.



Packaging must also be communicative. Through the process of human factor analysis, careful and detailed analysis identifies the key graphic elements and tools that form the basis for communicating key factors for success – instructions for patient use and administration, as well as conditions for safe storage or other drug protections, potential side-effects, and many others. Given the high value and critical nature of this category of medicines, compliance and adherence is vitally important for successful health outcomes. Leading pharmaceutical companies leverage the packaging system as an opportunity to address compliance and adherence by incorporating valuable patient support tools. In addition to well-prepared packaging graphics, it is common to include patient support tools such as brochures, leaflets and other included media that provide a platform for patient education, support programme enrolment, prescription discount or reimbursement, or other tools to address common factors for non-adherence.

Given the high value of the drug product and the inherent attractive nature of the drug category for counterfeiters or other bad actors in the supply chain, thorough preparation must also be given to a robust serialisation and anti-counterfeiting strategy. Taking a comprehensive approach in both the drug delivery device as well as the secondary packaging in a systems-based architecture provides an opportunity to orchestrate a multi-layered and nuanced strategy in ensuring ultimate product safety and authenticity, vital in today's global pharmaceutical market. This may require incorporating anti-counterfeiting elements in various parts of the delivery, as well as a rotational approach to the use and administration of these tools, to ensure the sophisticated strategy in staying ahead of criminal elements that may look to counterfeit or divert premium drug products.

Connectivity – the Next Frontier

As we transition between the era of the IoT and the advancing AI world, there is tremendous excitement in the world of connected health. Communication tools such as Bluetooth or NFC are simply the first stages in the ability of injectible devices being able to communicate proactively and reactively – both data gathering and transmitting for patient information, as well as inbound prompting and communicating – generating valuable new opportunities for interactivity in patient health. Benefits of such real-time connectivity include the ability to intervene when adherence issues begin to present themselves, as well as to deliver positive reminders and patient support in advance of bad habits being formed. Medication devices can be interconnected with other health monitors, related diagnostic devices, doctor and healthcare systems, and other touch points in the connected supportive healthcare ecosystem.

In Conclusion – a Bright Future for Amazing New Drugs

The industry has embarked on an exciting new journey, developing amazing new drugs for frustrating and long-term health issues such as diabetes, cancer and autoimmune conditions, demonstrating breakthroughs in combatting these afflictions and improving quality of life for those who suffer with the daily struggles of their diagnosis. Furthermore, incentives have provided a pathway for development of treatment for rare and orphan diseases, giving optimism to patients who may have otherwise felt lost and without hope of effective treatment, yet may now have therapy options that they never had before. There is optimism that biosimilars will level the playing field for a broad population of patients seeking impactful and affordable treatments.

Innovative new drug device technologies are making drug delivery increasingly safer and more effective, and are providing patients with new freedoms to live their lives – giving them more control and independence, without being bound by the requirement to constantly visit their healthcare provider for frequent treatment. Such advanced technologies allow them to live more normal and predictable lives. Even further advancing technologies may soon allow them to maintain a very connected health relationship with their providers without needing to be face-to-face. The advances in biotech medicine have transformed therapy and should provide hope and optimism to us all.

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