Enabling Competitive Entry: The Role of Drug Delivery Device Design in the Biosimilars Market

It is no mystery to the pharmaceutical and biotech industry that between 2018 and 2023, a number of original reference biologics will be coming off patent. This clearly opens up a significant window of opportunity for biosimilar manufacturers seeking to compete with the original biologics. Success, however, and market share gain will depend on a number of factors, including ease of adoption. We have specifically focused this article on analysing the different factors that will influence the uptake of new biosimilars and their advancing market share against original biologics, and dwell on the importance of optimal device design for combination products in this process.

Available Market Opportunity

The third and fourth waves of innovator biologic patents are set to expire in the next decade and the biotech industry is pursuing 106 biosimilars through clinical development for US and EU markets[1]. Currently, the EU has a greater number of approved biosimilars – 54 products[2]– than the United States (26 products[3]), yet expectations are that the number of biosimilars available today will represent just a paling fraction of what will be introduced in coming years[4].

In just the period between 2018 and 2023, seventeen biologics will have come off patent in Europe, and fifteen in the US. Our cautious estimate on the market opportunity represented in Europe for biosimilar manufacturers is $3.12 billion per year based on current revenues. The equivalent market opportunity in the USA comes to $5.24 billion per year. This is in spite of conservative modelling factoring competitive discounts and is based on 50% market share.

Competitive Pricing

The development of new biosimilars is expected to bring a reduction in the cost of biologics, appealing to belt-tightening healthcare systems and to patients often suffering from rare or orphan diseases. Biosimilars thus provide the opportunity to treat more patients earlier on, potentially averting the need for more expensive treatments in the future. As one study[5] notes, "…biologics may increase drug costs. However, biologics offer demonstrated improvements in patient care that can reduce expensive interventions, thus lowering net healthcare costs."

In fact, greater availability of drugs and choice provided by the entry of new biosimilars contributes to improving market competition and has been seen to generate price discounts that cluster around the 30% mark in Europe, in spite of some outliers[6].

These estimates are confirmed in the US, where one particular biologic that came out of patent in 2015 reveals that 25% has already been discounted off the branded reference drug pricing, and that the market expects this discount to increase a little further before settling into sustainable competition[7]. In the longer term, discounting of course needs to stabilise at a level that enables a sustainable market – where competitive market cost savings are balanced by reasonable commercial incentive for pharmaceutical manufacturers to continue investing in new drug discovery, development and regulatory approval.

Switching Pains

The process of switching patients from original biologics to biosimilars is a tricky one, surrounded by a number of both clinical and regulatory issues[8]. An important element is, of course, the lack of real-world evidence on which to base the decision by regulators to designate biosimilars as interchangeable. Independent studies[9] are beginning to add more significantly to the body of real-life clinical evidence that switching patients to biosimilars is effective and well-tolerated.

On the other hand, healthcare regulators, managers and clinicians around the world are keen to harness the cost reductions and wider access to treatment that biosimilar competition would enable. In the UK, NHS England are now urging a more proactive and collaborative approach between commissioners, providers and patients to realise the potential savings from switching to biosimilar medicines[10].

Successful uptake of biosimilars, however, depends on a number of critical factors that need to be considered by pharmaceutical companies and drug delivery device manufacturers alike. These include confidence in the biosimilar by patients and physicians alike, a more competitive pricing, and patient confidence in the drug delivery device where self-administration is indicated.

Smoother Switching: The Factors

One of the critical enablers post clinical judgement for a smooth switch between original biologic and biosimilar being raised by numerous commentators is the drug delivery device design: a growing volume of evidence shows that the design of what typically is an auto-injector or prefilled syringe for subcutaneous injection plays a critical role in facilitating switching[11]. In particular, the influence of drug delivery ease is noted in a number of studies and the FDA has made it a requirement that human factor studies are conducted to both support the device design and demonstrate that user-associated risks have been understood and mitigated.

Delivery of biologics is a particularly important element as larger molecule biological drugs tend to be more viscous, and also may present challenges with the volume of drug to be delivered as well as potential pain on administration, which may be frequent (weekly, for example). In addition to this, many healthcare systems are pushing towards self-administration within the home for chronic diseases to reduce the heavy burden on their systems and enable patients to access treatment without visiting a hospital. Patient usability therefore becomes of critical importance as it is both an important driver to encourage new users to adhere to their treatment plan, while existing users may also favour usability over habit, especially when suffering from degenerative diseases like Crohn's disease, ulcerative colitis, rheumatoid or osteoarthritis and many others.

Combination Products

New 'combination products' as designated by the FDA confirm the fact that the drug delivery device is an integral part of the

therapy, with pharma companies seeking exclusive arrangements with device manufacturers to gain competitive edge in the switching/retention process[12]. The FDA Office of Combination Products was established in 2002 and since then, combination products have had to adhere to a specific regulatory compliance pathway for approval and marketing authorisation in the US market[13]. To date, no such equivalent process has been established in Europe and these products are still granted approval for marketing authorisation by the European Medicines Agency (EMA) via the medicines approval route. This may change in the future with EMA currently reviewing the process[14].

The Devil is in the (Design) Detail

Analysis of both user and healthcare professional preferences[15] highlights the preferred delivery device or device platform design features and the series of steps that need to be taken to evaluate them. In sum, these reports show that:

Firstly, it is critical that the primary container is selected carefully. This initial evaluation should also take into account drug interaction and the impact of the container on drug stability, as well as its compatibility with the required manufacturing processes involved. Secondly, it is critical that regulatory compliance factors are taken into account right at the initial stages of design selection, particularly given the FDA's acknowledgement of the role of combination products and their specific set of compliance requirements. This phase will also require that design reviews are run and that human factor studies (as requested by the FDA) are undertaken. Device risk management considerations must be made in an organic and all-encompassing manner, and should include testing of development and qualification methods to provide accurate and realistic risk and confidence parameters.

Design Selection: Process is Critical

At this point, the selection of design and compliance features will have narrowed down to a restricted number of candidate devices that will need to be evaluated and tested further – on the following features as a minimum: robustness and usability based on target applications and patient population; assembly and manufacturing risk management; supply chain reliability; environmental/disposal risks and post-shipping device performance. Procedures for design control should also be put into place with fully documented design history file and a transparent design review process. Methods of operational transfer when required and post-market surveillance procedures also need to be considered.

Finally, the review of design selection shows that manufacturability and control strategy risk evaluation are increasingly important in helping businesses select the right device, along with packaging and shipping considerations. Access to device vendor site documentation, design control, risk management, design verification and validation are also critical in the device assessment and selection process. Device handling patient/user safety considerations also play a key role, and ISO10993 accreditation for biocompatibility of materials for cytotoxicity, irritation and skin sensitisation needs to be taken into account.

Conclusion

It is clear that the delivery device design is going to play an increasingly important role in the future of competition within the biosimilars market. With our estimates showing that the likely available market for biosimilar manufacturers seeking to compete with original reference biologics coming off patent between 2018 and 2023 is estimated to be $3.12 billion per year in Europe and $5.24 billion per year in the USA, close attention needs to be paid to device design to grasp upcoming opportunities. Successful uptake of biosimilars in fact depends on several factors, spanning from clinical confidence to competitive pricing and usability of the drug delivery device.

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