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AT THE HEART OF IT

Patient-centric drug development and clinical trial logistics

The concept of patient-centric treatment dates back to the 1950s, if not earlier, but it is now becoming a reality as the population of the Western world ages and chronic diseases become the main challenge for financially stressed healthcare providers. At the same time, other world markets are opening up to regional drug supply and a wide array of population-based drug development issues. Providers are increasingly shifting their focus from products to patients and are looking, above all, for the right outcomes rather than just purchasing drugs.

Pharmaceutical companies too need to focus more on holistic treatments than developing new drugs. They need to find new partnerships and new ways to collaborate with payers, providers and patients, and to combine the information they hold with that of caregivers. GSK, AstraZeneca, Novartis and Teva, for example, are some of the major pharma companies that have collaborated on the development of smart drug delivery devices.

The number of clinical trials has exploded in recent years; acording to the National Institutes of Health, the number has increased 33-fold since 2000. Trials are becoming more complex, last longer and involve more sites, while more and more of the drugs involved are biologics with complicated dosing regimens and administration protocols. An increasing number involve orphan drugs or others with limited patient populations, often in remote locations. Meanwhile, patients are more knowledgeable than ever before and are actively advocating for themselves. All this means that trials have to be designed around the needs of patients as never before.

PATIENT-CENTRICITY AND CLINICAL TRIAL LOGISTICS

Patient-centricity in pharmaceutical product development touches on the whole configuration of modern drugs from drug substance, to excipients, dosage, drug product and packaging, each of which can be formulated in many different ways to deliver a variety of medicines and treatments tailored to patient needs. That, however, is not enough: the process has to involve the whole of the clinical trial supply chain, including the logistics provider.

The direct-to-patient logistics solutions provider is crucial to the success of a complex clinical trial and is responsible for the entire process of getting material to and from every doctor and their patient in the trial. Clinical research associates are increasingly remote. For example, Marken's latest Sentry technology allows real-time online GPS tracking in addition to the monitoring of temperature, light, vibration and shock exposure. It also automatically sends texts to the final destination when the delivery is 10 miles (16 km) away, much like an Amazon delivery to a consumer.

Patient-centric services are extremely complex, because clinical trials are extremely complex. Often, they take place across multiple regions and with accelerated and constrained timelines, frequently involving low volume products. Although many logistics companies can deliver shipments door-to-door, and provide international shipping, this is about far more than just delivering a drug to a doctor's office or a patient's home address. Marken is the only supply chain organisation solely dedicated to clinical trials; the one who interacts with the patient during a trial — other than their doctor — leading the way in direct-to-patient services.

"In both 2014 and 2015, more than 40% of the novel drugs approved by the US FDA were destined to treat orphan or rare diseases"

DIRECT TO PATIENT (DTP) HOME DELIVERY

With Marken's Direct to Patient (DTP) Home Delivery Service, clinical trial materials are delivered direct by trained drivers — from investigator sites, pharmacies or depots — to the patient's home. The company has also partnered with a worldwide nursing care network, which is active in more than 45 countries, to conduct study visits at patients' homes, offices or holiday destinations. This, to Marken, is all part of the true definition of being patient-centric. It means that patients in trials, who are usually already seriously ill and may well have difficulty travelling, are spared the need to go to a clinic, which may be a long distance away, to have their treatments administered.

If necessary, which is particularly often the case with biologics, the drugs used in the trials have full temperature monitoring from pick up to delivery. Where individual treatments are involved, such as in the case of cell therapies, there is a chain of individual identity from the moment the cells are taken to when it becomes an active pharmaceutical ingredient (API). This is all part of Marken's focus on improving the lives of patients.

CELL AND GENE THERAPIES

We believe strongly that cell and gene therapies, which are patient-centric by definition, will be the future for Marken, and the requirement for logistics with very strong communication pathways will play to our strengths. Estimates are that more than 250 companies have initiated cell therapy trials this year (2016), while there are 435 cell therapy trials ongoing.

At the moment, very few contract development and manufacturing organisations (CDMOs) are active in the field. These companies, most of whom Marken has worked with, understand the challenge of taking these new therapies from clinical to commercial in a global market. It will take time for related service providers to implement new manufacturing and delivery technologies, and we will be available to provide insight and support in related clinical trial logistics.

SPECIAL DESIGNATIONS

The move towards patient-centric drug development is linked to a large degree with the shift towards orphan drugs, those defined by the US Orphan

Drugs Act of 1983 as intended to treat fewer than 200,000 people. This act has been followed by similar legislation in the EU, Japan, Singapore and Australia. Incentives such as tax breaks and exclusivity are also reviving interest from large pharma companies in therapies that were too limited to fit the blockbuster model in the past.

The result of all this has been that the number of orphan drug indication designations has grown from just 38 to more than 400 since 1983. Evaluate Pharma's Orphan Drug Report of 2013 forecasts that the market will grow by 7.4%/year to reach $127 billion by 2018, far outstripping the growth of the overall prescription drug market (generics excluded) and reaching 15.9% of the market in that year, more than treble the share they had in 1988. In both 2014 and 2015, more than 40% of the novel drugs approved by the US FDA were destined to treat orphan or rare diseases.

Orphan drugs are inherently more likely than mass market drugs to be developed in a patient-centric way, and to have a more widely dispersed patient base, because of the relative rarity of the conditions they treat. They are also more likely to be complex drugs, be they synthetic or biological. Conversely, orphan drugs do not benefit from any relaxed trade compliance procedures. On the contrary, their import and export is subject to the same regulatory scrutiny as any other drugs, approved or unapproved, even when used in clinical trials. In this context, the role of the logistics provider is even more important.

The same observations apply to other special drug designations, including Fast Track and Breakthrough Therapy. Manufacturing processes have to be developed as per the normal process, but safety and efficacy data must be generated in much less time than with conventional drugs, for smaller and more challenging patient bases, and all without compromising safety in any way.

MANAGING BRIGHT STOCK

At the moment, in many countries, unlabelled product cannot be delivered to a depot for use in a clinical trial. When there is a trial in multiple countries, the material needs to be packaged, labelled and stored even before patient recruitment begins, and there is no way to know or control the numbers of patients that can be recruited or where they will be. The end result is that pharmaceutical companies might destroy more than 50% of the drug product in the trial, which is wasteful and causes delays.

Marken has been working with pharmaceutical companies and CDMOs to allow 'bright stock' with a label only on the outside package, which verifies where the product was created. This has two key advantages: product would always be available when and where needed, and the amount of waste would be reduced. A vial could be labelled and delivered via the depot to the patient within 24 hours.

Marken also works with e-labelling companies. Technology is now available that's similar to that on an e-reader, so that it's possible to radio-transmit changes to a label within a depot. For example, if a drug has limited stability but new stability data emerges and is validated, the label could be changed electronically. This is being trialled at our Frankfurt warehouse and will go live at another in Singapore. The potential is tremendously exciting.

CONCLUSION

Patient-centric pharmaceutical development has recently moved from a hypothesis to a reality. It fits with what healthcare providers are looking for, while both technological advances and the industry trend to integrated CDMO services are helping to make it happen. Above all, though, this is a labour-intensive logistical exercise that requires an international base and a wide range of capabilities from the logistics providers. Issues such as patient confidentiality and labelling still have to be ironed out in many countries; but, when they are, the future will be bright.

FOR MORE INFORMATION

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