Going the Extra Mile: The Role of Temperature-controlled Packaging in a Patient-centric Supply Chain

Getting the right medicine into the hands of a patient in a timely manner has always been the ultimate goal in the clinical supply chain. As the pharmaceutical industry moves away from the 'blockbuster era' into biologics and personalised medicines, the challenge of maintaining a controlled supply chain, from production to the time of administering the medicine, becomes even more complex.

Historically, drugs are manufactured for the wider population and are prescribed using statistical averages: these work for the majority of patients but not all. In fact, generally, any given prescription drug on the market only works for half of those who take it. While this can be attributed to genetic differences among the population, these days, diagnosis has become more accurate due to testing for genes known to be associated with some diseases.

This has paved the way for personalised medicines (also known as precision or stratified medicines), which are based on each patient's unique genetic makeup and are beginning to overcome the limitations of traditional medicine.

Getting Personal

Personalised medicines rely on technology that confirms a patient's fundamental biology, DNA, RNA, or protein, which leads to confirming diseases. Individual techniques such as genome sequencing can reveal mutations in DNA that influence diseases ranging from cystic fibrosis to cancer. For example, the FDA-approved drug, Ivacaftor, for the treatment of cystic fibrosis (CF), will help up to 4 % of cystic fibrosis suffers and may eventually prove to be an important step towards better treatments for all CF patients[1].

Associated with the development of personalised medicines, the industry is moving from long chain molecular pharmaceuticals into what is commonly referred to as biological pharmaceuticals or biologics, which have been billed as one of the biggest changes to healthcare in recent years. Currently, it's estimated that a third of all pharmaceutical industry research and development is spent on biologics[2] and by 2018, sales from biological medicines are set to increase to 49 per cent by revenue of the world's top 100 drugs (Strickland and Raeside, 2012).

Due to the sensitive nature of biologics, for most clinical trials now, there is a much higher chance that the investigational medicine products (IMPs) are going to be temperature-controlled to ensure their efficacy. They also need a much colder supply chain (2–8°C), as they are inherently less stable than long molecular drugs. Indeed, it's not just the manufacturing of IMPs that pose a challenge, but the appropriate storage, transportation and distribution of these sensitive products that can perhaps play the most important role in protecting their integrity. The dissemination of products during clinical trials needs to be carefully planned and managed, because one solution does not suit all situations. Due to the temperature-sensitive nature of biologics, the transportation during the 'extra' mile, from pharmacy or hospital setting to the point of patient administration, can prove even more difficult to manage.

Compliance

To maintain medicine integrity, temperature-sensitive drugs, such as insulin and vaccines, require storage at a controlled temperature (2–8°C) with protection from freezing. Deviations outside this temperature range can compromise medicine efficacy, resulting in therapy failure. For example, at 0°C vaccines can freeze and become deactivated or at temperatures above 8°C, their potency may be compromised. As well as the implications of wastage of medicines, inaccuracies with trials can represent a considerable financial loss to pharmaceutical companies.

The updated GDP guidelines mean that tighter regulations are in force when it comes to the storage and distribution of temperature-sensitive products and all products need to be transported to the label claim. Where previously, throughout the entire cold chain, you could rely on the stability data to justify why an element of the cold chain wasn't as strict as it should be.

As a result of the GDP guidelines, cold chain models have changed and there are now more warehouses at airports, so temperature-controlled packaging is not challenged as much as it used to be: temperature excursions are now an exceptional circumstance rather than expected.

Conversely, shipping/distribution regulations vary widely from country to country, and uniform guidelines are lacking. This divergence has proved challenging for the pharmaceutical industry. Generally speaking, pharmaceutical distributors are aware that they need to be GDP-compliant to ensure their product gets to the end point safely. However, there is little information in the guidelines on how to achieve this: and this is where temperature-controlled packaging manufacturers need to take the lead. It is the role of the temperature-controlled packaging manufacturers to have the knowledge on what is needed to be compliant and to maintain the efficacy and quality of the product being shipped.

However, while transport and delivery of temperature-controlled products to the end user in a hospital or pharmacy setting is covered by GDP, the process can be even more challenging for clinical supply managers who need to deliver directly to patients as part of the growing trend of direct home delivery. This 'extra mile', which represents taking the medicine home and its storage, is not included and currently, without this cover the chances of the drug not being as effective could be quite high.

Home Delivery

Another reform in healthcare is an increased emphasis on self-administration of medicines, both in hospitals and at home. A number of studies have demonstrated that if you give patients more knowledge and control, they will have a better understanding of their healthcare pathway and compliance will increase.

This means that there is an increased likelihood that a drug is going to be given to an individual end user to store or transport, rather than sent to pharmacy or hospital to be given straight away. So as patients are more likely to be taking medicines home, it stands to reason that they should require temperature-controlled packaging for this journey. Currently, as there is no guidance to cover this 'extra mile,' a high-value, life-saving, temperature-sensitive medicine would be governed under strict 2-8°C temperature control until it enters the pharmacy fridge and then the pharmacist puts it in a paper bag and sends a patient on their way, which increases the risk of damaging the drug and rendering it useless.

Previously, with long molecular drugs, even if they need to be kept refrigerated, they could be left out of their temperature range for up to a week without it really harming the effectiveness, but the new biologics are a lot more vulnerable. Patients would have no way of knowing if a temperature breach has occurred, resulting in the drugs being compromised. So with this 'link' missing, how are these products protected from ambient temperatures, which could damage the product if the patient has a long journey home, or is going out for the day or on holiday?

Indeed, when travelling by plane, whether on holiday or business, there are restrictions on the amount of liquids you are able to take in the cabin with you. There are exemptions available for medicines and the coolpacks used if necessary, however, there are instances where it is specified that coolpacks need to be solid, but if a patient has a long journey to the airport and in a warm

climate, it is unlikely that the packs would remain entirely solid. The current guidance available is also very varied when comparing the UK government website to that of airlines and, with that in mind, there will not be global harmonisation either.

As more people are likely to encounter this in the future, this is certainly an area that needs clarification, both for patients and for manufacturers. With clearer regulations and guidance in place, temperature-controlled packaging can be designed accordingly, to combat issues in advance.

Temperature Control

Temperature-controlled packaging manufacturers have developed systems for the patient to protect medicines during these types of situations. These patient-centric temperature-controlled packaging products are much smaller than traditional temperature-controlled systems, as they are designed for a single pack, dose, or smaller quantities, compared to most boxes that are designed for moving large amounts of products around. They are also much more patient-friendly, so will be fitted with handles, zips etc. and use PCMs with a year-round pack out, rather than summer and winter configurations. They are also designed specifically for the patient to address any limitations. For example, if the medicine is to help arthritis, the packaging would be designed for someone who couldn't use their fingers very well, so they can open, prepare, and use it.

These have been used in select clinical trials where patients are given a patient pouch to transport and keep control of their medication. However, once the trial is finished and the product becomes a publically available drug, that support isn't currently available. This is largely due to financial prohibitions, as it would be costly to give each patient that is prescribed the medicine a temperature-controlled packaging system. Plus, who is responsible for the cost? The drug company, medical insurance, the NHS, the patient?

Some speciality pharmacists do use thermal shipping methods to get temperature-sensitive medicines into the hands of the end user. These include insulated bubble bags, insulated envelopes or coolers that claim to maintain a temperature for up to 24 hours. However, a recent study of these systems[3] outlined that these methods performed below average, which resulted in the transported drugs' temperature breaching the predetermined threshold. This highlights the need for more robust and secure packaging methods for this 'extra mile' distribution.

Conclusion

Currently, healthcare professionals, patients and most retailers are, by and large, unaware of the challenges experienced in the cold chain during this 'extra mile.'

There is unquestionably a need for a collaborative approach to address this issue. In clinical trials, pharmaceutical companies have been the driving force in protecting the 'extra mile' as part of their protocol, but of course this is more tangible in a clinical trial setting because 100 per cent compliance needs to be ensured. When it comes to a finished pharmaceutical, the profit margin comes into play and additional costs, which are outside of regulatory compliance, are often not a consideration.

While it is clear that a one-size-fits-all approach is no longer the way forward, there are best practice methods that can be employed to ensure patient safety and product integrity. Knowledge is key when it comes to global transport and understanding the challenges that lie ahead, including local regulations. However, it doesn't stop there, because as biologics and patient-centred medicines continue to rise, the extra mile from pharmacy to home will play an increased role in ensuring the clinical cold chain remains intact.

References

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