Drugs shortages are finally being addressed

Maintaining the security and quality of the manufacturing supply chain for drug products is a significant responsibility for all marketing authorisation holders (MAHs) to ensure the sustained availability of medicinal products for human use. There is clear proof that interruption of medicinal product supply can lead to treatment failures and the use of less appropriate, and often more expensive, alternative drugs. Disruptions to supply or delayed treatment also increases the potential for dispensing errors and lowers patient compliance. A rise in occurrences of largely preventable adverse events associated with alternative treatments is also seen.

Recent unanticipated interruptions to the pharmaceutical manufacturing supply chain due to manufacturing/GMP compliance issues have resulted in both acute and chronic scarcities of important medicinal products across the EU and the US, necessitating modifications to prescribing information, and commencement of patient allocation programmes.

EU regulations require the compulsory pre-notification by MAHs of any disruption of supply caused by manufacturers of medicines in the case of any quality issues that could lead to an unexpected restriction in supply or when there are permanent or temporary cessations of supply. Similarly, the US Food and Drug Administration (FDA) has recently published a draft 'Interim Rule' regarding modified compulsory supply. Similarly, the US Food and Drug Administration (FDA) has recently published a draft 'Interim Rule' regarding modified compulsory pre-notification requirements for manufacturers of medicines in case of potential drug shortages.

The FDA has indicated that the vast majority of drug shortages involve generic drugs, particularly well established, sterile drug products. In a minority of cases drug shortages involve innovator products. Some of the reasons include raw material shortages, shifts in clinical, wholesaler or pharmacy inventory practices, changes in distribution process, natural disasters, regulatory issues (including changes in regulatory guidance), manufacturing challenges and decisions by companies to discontinue specific products. Indeed, sometimes drug shortages can affect the supplies of alternative drugs. In the US, the Drug Shortage Program works with the manufacturer to mediate the problem. The FDA cannot mandate manufacturers to either resume or increase production to alleviate drug shortages, but they can provide assistance, whether the shortage is caused by voluntary recalls, cGMP issues, or even business decisions.

The International Society for Pharmaceutical Engineering (IPSE) recently published a Drug Shortages Prevention Plan which was aimed at providing guidance for the pharmaceutical and biopharmaceutical industries on how to establish reliable, robust and resilient supply chains that can, without interruption, provide quality medicines to patients. This plan was the result of a cross-industry initiative in response to a request from the European Medicines Agency in 2013 to address the issue of drug shortages caused by manufacturing and/or quality issues.

The plan utilised the outcome from an earlier drug shortages survey to facilitate developing strategies to prevent drug shortages. It is focussed on six key areas, ‘corporate quality culture, robust quality systems, metrics, business continuity planning, communication with regulatory authorities and finally, building capability’. IPSE hoped that it would be useful to the industry, helping them to look holistically across their supply chain and challenge them to assess their own strategies for meeting current challenges, or indeed whether changes are required and existing processes improved. It was viewed as a ‘toolbox’ whereby industry could select the appropriate tool for the most applicable problem.

In addition, the Parenteral Drug Association (PDA) in collaboration with EMA has introduced advice on risk-based prevention of drug shortages. This involves a risk based ‘triage’ of impacted products based on the criticality of the product and patient impact. This is then followed by a product risk register and a drug shortage prevention and response plan.

Finally, the European Federation of Pharmaceutical Industries and Associations, European Generic Medicines Association, Association of the European Self Medication Industry and Plasma Protein Therapeutics Association collaborated on issuing a white paper on quality- and manufacturing-driven supply disruptions, including harmonised communication principles with a reporting framework and time points for formal notification.

Overall, it is clear that drug shortages are a problem for all parties concerned, particularly patients. However, it is equally clear that this issue has prompted a remarkable degree of collaborative effort and it is to be hoped that this issue can be fully addressed in the near future.

References

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