New rules in China tighten ADR reporting environment

Katherine Wang discusses the new reporting rules on adverse drug reactions.

Revised rules on reporting and monitoring adverse drug reactions in China are due to come into effect on 1 July[1].

The new ADR rules significantly increase the regulatory requirements on pharmaceutical manufacturers and place new obligations on regulatory authorities. Comprising eight Chapters and 67 Articles, they are more prescriptive and detailed than the rules they replace.

Multinational companies marketing their drugs – whether domestically produced or imported – in China are advised to review their standard operating procedures and reporting structures. Given that regulatory obligations in China differ from those in Europe and the US, it will be critical for firms to assess to what extent the revised rules will impact their global drug safety management systems and to adapt these to the new statutory requirements.

The primary responsible party

The revised ADR reporting rules were issued by the Ministry of Health on 4 May. They require drug manufacturers to establish a management system for monitoring and reporting adverse drug reactions. Manufacturers must proactively collect any information related to ADRs and record details thereof for analysis and handling. They must also co-operate with drug regulatory authorities during the investigation of ADRs. In the event of an ADR involving death, in addition to the existing reporting obligation, the manufacturer will have to complete an investigation within 15 days of learning of the event and submit the investigation to the provincial Food and Drug Administration where the manufacturer is located. Manufacturers must also prepare periodic safety update reports, or PSURs, summarising domestic and foreign drug safety information about their products and analysing associated risks and benefits.

Under the reporting rules, manufacturers must proactively initiate drug safety studies based on the analysis and evaluation of ADR reports and monitoring data. Where a drug is confirmed with serious ADRs, the manufacturer has to take a series of remedial measures. These include communicating with physicians, patients and the general public; disseminating warning information; revising labels; and suspending the manufacture, distribution and use of the drugs in question.

More importantly, manufacturers will have to evaluate regularly the safety profiles of their drugs and place new products within their statutory monitoring period (ie five years from the date of marketing approval or the first importation) under priority monitoring. Data collected during the priority monitoring period must be summarised, analysed, evaluated and reported. The State Food and Drug Administration and provincial FDAs can also require manufacturers, national or provincial ADR centres, healthcare institutions or scientific research institutions to place certain products under priority monitoring based on data collected through clinical practices or the ADR reporting system.

In addition to being subject to monetary fines ranging from RMB5,000-30,000 ($771-4,625) for violations of the above regulatory obligations, manufacturers may also be prohibited from renewing the marketing authorisation for their products should they fail to submit PSURs or implement priority monitoring.

Changes in reporting requirements

The revised rules set two different reporting paths, one for single-case ADRs and one for mass ADRs. Single-case ADRs must be reported through the online ADR surveillance system designated by the National Center for ADR Monitoring or to the ADR centres where reporting manufacturers, distributors or healthcare institutions are located. Mass ADRs must be reported to the drug regulatory authorities at county level as well as to health authorities and ADR centres where the reporting manufacturers, distributors or healthcare institutions are located. For imported drugs, the manufacturer must report serious ADRs that occurred outside China to the National Center for ADR Monitoring.

The timelines for reporting serious or new ADRs (15 days) and ADRs involving death (immediately after learning of the event) remain unchanged under the revised rules. However, the timeline for "regular" ADR reporting has been shortened from three months to 30 days.

Evaluating and investigating ADRs

While the previous reporting rules mainly addressed the ADR reporting process, the revised rules in addition require drug regulatory authorities to analyse, evaluate and investigate ADRs in order to establish a risk-based management system. Specifically, ADR centres at city or county level must verify the accuracy, completeness and preciseness of single-case ADR reports and produce an evaluation report within 15 days (or within three days for serious ADRs); they must complete investigations of ADRs involving deaths within 15 days of obtaining the relevant ADR reports and submit the investigation reports to drug regulatory authorities and health authorities at the same level and higher level ADR centre. Higher level ADR centres will have to analyse and evaluate the opinions from lower-level ADR centres on serious ADRs or ADRs involving deaths.

In the event of mass ADRs, drug regulatory authorities at city or county level must organise on-site investigations jointly with health authorities and report the findings to higher-level drug regulatory and health authorities. Higher-level drug regulatory and health authorities may direct and supervise the on-site investigations, or organise such investigations for mass ADRs with a larger impact.

Provincial ADR centres and the National Center for ADR Monitoring must, respectively, conduct analyses of ADR and serious ADR reports on a quarterly basis, identify and evaluate noteworthy drug safety information and propose risk mitigation measures to drug regulatory and health authorities. Drug regulatory authorities may suspend the manufacture, distribution and use of drugs based on the evaluation of associated ADR reports. They can also demand changes in drug labels, or they can recall, or revoke, a marketing authorisation based on the evaluation of associated serious ADR reports.

Some lack of detail

The revised rules expand considerably the regulatory obligations for pharmaceutical manufacturers. Despite the emphasis on investigation and evaluation of ADRs, however, they lack detail about how manufacturers and regulatory authorities should conduct the investigations and evaluations. The type of information that manufacturers are expected to record in an ADR investigation report is not clearly stipulated and it remains unclear whether the findings in an ADR investigation report could be used to determine liabilities for injuries or loss of life caused by the drug in question.

Drug firms doing business in China should define an internal standard operating procedure for the reporting, investigation and evaluation of ADRs and closely monitor the enforcement practices of competent regulatory authorities to ensure full understanding of and compliance with the new requirements.

References

1. *SFDA press release, 25 May 2011, http://eng.sfda.gov.cn/WS03/CL0757/62683.html*

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