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Regulatory assessment of pandemic (A)H1N1 influenza vaccine and narcolepsy safety issue: lessons for resources limited countries

Y.J. Doua[1,2], H. Dominicus[1,3]
1 Consortium for African Regulatory Expertise Development (CARED), Voorburg, The Netherlands
2 Benelux Pharmacovigilance Office, Global Medical Organization, Johnson&Johnson
3 Dominicus Medicus Consultancy, Voorburg, The Netherlands

Background:
Rare but serious adverse events (SAE) may pass clinical trial phases unobserved. To assure that SAEs are captured in post-approval, pharmaceutical companies and regulators are required to put pharmacovigilance systems in place. Unfortunately, pharmacovigilance infrastructures are still very weak in most resources limited countries in Africa.

Aim:
To help raising safety awareness for regulators and society, we reviewed the narcolepsy and pandemic (A)H1N1 influenza vaccine issue by highlighting the strengths and weaknesses of pharmacovigilance.

Results:
In August 2010, following widespread vaccination against (A)H1N1 pandemic, serious cases of narcolepsy were reported worldwide notably in Nordic European countries. After review, the European Medicine Agency (EMA) required more data to clarify the emerging safety concern. A Finnish nation-wide observational study showed a 17-fold increased risk of narcolepsy in children and adolescents few months after vaccination compared to that before. The Finnish and Swedish authorities withdrew the vaccine while the EMA required additional data to exclude potential bias. The European Center for Disease Control found for narcolepsy and the vaccine an Odds ratio (OR) of 14.2 (95%CI 2.5–infinity) in Nordic countries (in non-Nordic countries OR=2.3 (95%CI 0.9–6.3)). Although a conclusion on causality was not finalized, based on these results EMA preventively excluded persons under 20 years from the use of the vaccine.

Conclusions and Recommendations:
This narcolepsy case underlines the importance of appropriate routine SAE reporting in identifying safety signals. For a robust vaccine risk assessment however, additional pharmacovigilance tools such as pharmaco-epidemiology studies are necessary. To reliably monitor medicines safety, African hospital records and epidemiological disease surveillance need improvements to gather background incidence of serious conditions. Additionally, pharmaco-epidemiology research abilities should be promoted alongside the African regulatory harmonization and strengthening initiative. Neglecting these measures would impair the regulatory efficiency and thereby adversely affect access to quality-assured medicines for patients.