CHARACTERISTICS OF VACCINES ON SERBIAN MARKET IN TERMS OF PRESENCE OF POTENTIALLY HARMFUL EXCIPIENTS

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INTRODUCTION: Vaccine use is often reduced due to concerns for their safety. In addition to the active pharmaceutical ingredient (API), the question of safety of all other ingredients that make up the pharmaceutical-technological formulation of vaccines is raised. Preservatives are the most common group of excipients that can be potentially dangerous, but it is now known that other classes of excipients can cause non-API related adverse drug reactions (ADR).[1]

OBJECTIVES: The aim of this study was to identify potentially harmful excipients that are part of vaccines that marketing authorization received from the Medicines and Medical Devices Agency of Serbia (ALIMS).

METHOD: This study was conducted in October of 2021. Qualitative content of vaccines registered in Serbia was observed from Summaries of product characteristics (SmPC) available at official website of ALIMS. Sections 2. and 6.1. were observed. Excipients were considered potentially harmful if they were listed as excipients with known effect (EKE) in European regulation, Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'[2] from official website of European Medicines Agency (EMA).

RESULTS: A total of 64 SmPCs were analyzed ant the results are shown in Table 1.. Each of analyzed SmPCs showed presence of at least one EKE in vaccine formulation. Most of the analyzed SmPCs did not contain information about quantitative content of excipients, EKE included.

Table 1. EKE present in analyzed vaccine SmPCs

EKE according to EMA	Number of analyzed SmPCs in which EKE is present	Comment
Sodium compounds	61	In form of sodium chloride, sodium hydroxide, sodium bicarbonate, sodium borate, sodium citrate, sodium dihydrogen phosphate, sodium hydrogen phosphate, disodium adipate, edetate disodium
Potassium compounds	22	In form of potassium chloride or potassium hydrogen phosphate and potassium dihydrogen phosphate as part of the phosphate buffer
Phenylalanine	19	In 16 formulations as part of *Hanks medium 199;* ALIMS also singled it out as EKE in 10 analyzed SmPCs *in two analyzed SmPCs (other than 19 with listed phenylalanine) amino acids are listed as excipients, which could potentially include phenylalanine
Glucose	17	In 16 formulations as part of *Hanks medium 199*
Ethanol	13	ALIMS also singled it out as EKE in 10 analyzed SmPCs
Sorbitol	7	ALIMS also singled it out as EKE in 7 analyzed SmPCs
Thiomersal	4	ALIMS also singled it out as EKE in 4 analyzed SmPCs
Sucrose	17	EMA recognized it as EKE only for oral route of administration; nevertheless, ALIMS did label it as EKE in section 2. in three vaccine SmPCs, even stating quantitative content

CONCLUSIONS: The analysis of SmPC documents showed that all vaccines on the Serbian market contain at least one EKE. Particular caution should be exercised with thiomersal-containing vaccines as this EKE may cause the most severe ADR of all detected EKE - allergic reactions. Also, EKEs that interact with other drugs (ethanol in 13 vaccines) and that indicate contraindications for the use of vaccines (phenylalanine in 19 vaccines) have been detected. The effect of EKE is in most cases dose-related, and as these data are often not available in SmPC documents, no definitive conclusions can be drawn about the potential harm. All detected EKEs are completely safe for the vast majority of patients.

REFERENCES:

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