Excipients with potential to cause adverse drug reactions in approved hormonal medicines for systemic use

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INTRODUCTION:

In addition to the active pharmaceutical ingredient (API), the composition of the medicines also includes excipients which are only ideally completely pharmacologically inactive. It has been shown that excipients can cause effects opposite to the pharmacological effect of the medicine. Therefore, it is very important to talk about excipients with known effect (EKE), which are excipients that have been proven to cause adverse drug reactions (ADRs) when they are in the composition of medicines.

OBJECTIVES:

The aim of the study was to identify potentially harmful excipients in hormonal medicines for systemic use approved in the Republic of Serbia.

METHODS:

The study was conducted during August 2021 and included the analysis of medicines that received a marketing authorization from the Medicines and Medical Devices Agency of Serbia (ALIMS). Qualitative compositions of hormonal medicines for systemic use (ATC group H) available in SmPC documents on the ALIMS's official website were observed. Excipients considered potentially harmful if they are recognized 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’, available from European Medicines Agency's official website.

RESULTS:

We analyzed 92 hormonal medicines for systemic use that are approved in Serbia. In their composition we found 70 different excipients. By comparing detected excipients with appropriate European regulation we identified 21 excipients from examined preparations that represent potential causes of ADRs: phosphate buffers (8 different buffers), mannitol, benzyl alcohol, benzalkonium-chloride, lactose-monohydrate, sodium, ethanol, glycerol, propylene-glycol, glucose, sodium-laurilsulfate, butylated hydroxytoluene, methyl p-hydroxybenzoate and propyl p-hydroxybenzoate.

CONCLUSIONS:

It has been shown that most detected EKE can cause mild ADRs after oral and parenteral administration such as irritation, headache, abdominal pain, mild diarrhea and allergic reactions (most often due to intolerance), while some excipients such as benzalkonium-chloride, sodium-laurilsulfate, phosphate buffers and butylated hydroxytoluene by the given method of administration do not cause any side effects. In addition, it has been shown that mannitol (34/92), lactose-monohydrate (27/92) and sodium compounds (21/92) are the most common excipients in composition of hormonal medicines for systemic use.

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