

## **ABSTRACT**

### **Analysis of utilisation and spontaneous adverse events reports related to human papillomavirus vaccines**

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**INTRODUCTION:** HPV vaccination is one of the most effective types of prevention against the human papillomavirus infection that can lower the probability of its incidence up to 80-90 %. Besides the benefits of vaccination, there can also occur among many individuals certain risks and adverse effects. Spontaneous adverse events reports are used to identify these serious and unexpected adverse effects, their monitoring leads to increasing safety of therapy. Drug consumption is monitored to uncover the ratio of population exposure to certain drug during specific time in specific socioeconomic group.

**OBJECTIVE:** The objective of this diploma was analysis of spontaneous adverse events reports of vaccines against the human papillomavirus that are registered in database of State Institute for Drug Control in the period from May 2007 to October 2017. Another aim of this work was to evaluate consumption of HPV vaccines in the Czech Republic in the period from 2006 to 2019 using data from State Institute for Drug Control again.

**METHODS:** Within the framework of analysis of spontaneous adverse events reports that were obtained from Central Database of Adverse Events Reports that is led by State Institute for Drug Control, only reports with ATC group J07BM were evaluated. Programme MedDRA was used to classify adverse effects to organ systems. The data like age, age group and gender of patient, specialism and number of reporting people, then information about way of reporting or reporting region, way of vaccination use, reaction outcomes, severity of adverse events reports and their expectability. These data were compared to information from Summary of Medicinal Product Characteristics. Method of DUR (drug utilization review) was used to study consumption of HPV vaccines in the Czech Republic. The subject of its study were data with ATC group J07BM. Final consumption was expressed in the number of packages and overall consumption in the certain

period and consumption of HPV vaccines in every single year were evaluated. Programme Microsoft Office Excel was used to process the results into the charts and graphs.

**RESULTS:** Generally 159 reports including 498 adverse effects were reported. The most common adverse effects that occurred in patients belonged to organ systems „General disorders and administration site conditions“ (21,69 %), „Nervous system disorders“ (18,90 %), „Skin and subcutaneous tissue disorders“ (8,23 %), „Musculoskeletal and connective tissue disorders“ (7,23 %) and „Gastrointestinal disorders“ (7,23 %). Vaccine Silgard was characterized by the highest number of adverse events reports, then Cervarix and Gardasil 9. Children that were 13-17 years old (35,2 %) were the most commonly included in reports, women were included in 96,85 % of all reports. Serious adverse effects were included in up to 89,3 % of all reports. No adverse effect led to death, not even to temporary or permanent disability. Unexpected adverse effects were included in 59,8 % of overall number of adverse effects. Consumption of HPV vaccines Silgard and Cervarix had been increasing since the date of their registration, since 2011, consumption had started decreasing gradually. The highest consumption of HPV vaccines was in 2010. Since the date of registration of vaccine Gardasil 9, its consumption has been increasing every year. Since 2018, overall consumption of HPV vaccines has started increasing slightly again. In overall the most common utilized vaccine was Cervarix (828846 packages), then Silgard/Gardasil (762543 packages) and Gardasil 9 (83511 packages).

**CONCLUSION:** During the analysis of adverse events reports, information about the most frequent, serious and unexpected adverse effects after HPV vaccination were collected. Despite the fact that serious adverse effects created a big part of all adverse effects, the most of them have disappeared, none of them was fatal. Local reactions after vaccine application, nausea, fever, headache, vertigo and fatigue were considered as expected occurring adverse effects. According to Summary of Medicinal Product Characteristics and available sources, HPV vaccines are considered to be safe and well tolerated. Consumption of vaccine Cervarix equaled to 828846 packages, vaccine Silgard/Gardasil's consumption equaled to 762543 packages and the newest vaccine Gardasil 9 was matched to 83511 packages. For the last few years consumption of vaccines Cervarix and Gardasil had been decreasing gradually even the overall consumption had been decreasing, the cause of that all could be mistrust of patients in safety of vaccines. However, since 2018, overall consumption of HPV vaccines have been increasing again.

**KEY WORDS:** spontaneous reports, drug consumption, HPV, vaccination, adverse effects