Drug Safety NEWSLETTER
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IRISH MEDICINES BOARD

Human papillomavirus (HPV) Immunisation Programme

Background

Two vaccines, Gardasil ® and Cervarix ®, are licensed for use in Ireland and across the EU for the prevention of high-grade cervical intra-epithelial neoplasia (CIN grades 2 and 3) and cervical cancer associated with HPV types 16 and 18. These vaccines have been shown to be effective in preventing cervical dysplasia (the condition that can lead to cervical cancer) in follow-up studies over a five-year period in women that did not have HPV at the time of vaccination. Vaccination against HPV, therefore, provides the potential to reduce the incidence of, and mortality from cervical cancer.

The Product Information (Summaries of Product Characteristics and Package Leaflets) for these centrally authorised vaccines is accessible via the IMB and EMA websites http://www.imb.ie and http://www.ema.europa.eu .

The IMB understands that a school immunisation programme using the HPV vaccine, Gardasil, is due to commence in the near future and the use of Gardasil will be in accordance with national immunisation recommendations (see www.immunisation.ie for additional information) as provided for in the Summary of Product Characteristics.

Gardasil

Indication: Gardasil is a vaccine for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18 (see section 5.1 of the Summary of Product Characteristics). The indication is based on the demonstration of efficacy of Gardasil in adult females 16 to 26 years of age and on the demonstration of immunogenicity of Gardasil in 9- to 15-year old children and adolescents.

Posology and administration: The primary vaccination series consists of 3 separate 0.5 ml doses administered according to the following schedule: 0, 2, 6 months. If an alternate vaccination schedule is necessary, the second dose should be administered at least one month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should be given within a 1-year period. The need for a booster dose has not been established. There is no experience with the use of Gardasil in children under 9 years of age (see section 5.1 of the Summary of Product Characteristics). The vaccine should be administered by intramuscular injection. The preferred site is the deltoid area of the upper arm or in the higher anterolateral area of the thigh. Gardasil must not be injected intravascularly. Neither subcutaneous nor intradermal administration has been studied. These methods of administration are not recommended (see section 6.6 of the Summary of Product Characteristics). It is recommended that individuals who receive a first dose of Gardasil complete the 3-dose vaccination course with Gardasil (see section 4.4 of the Summary of Product Characteristics).

Safety Profile: Gardasil has been authorised for use across the European Union since 2006, with significant post-marketing experience both within and outside the EU. The most commonly occurring side-effects initially identified from clinical trial data are consistent with those observed post-authorisation to date and are listed in the product information. The vast majority of suspected adverse reactions have related either to the signs and symptoms of recognised side effects listed in the product information or were due to the injection process and not the vaccine itself (i.e. 'psychogenic' in nature). Worldwide, over 54 million doses of Gardasil have been distributed. With this number of people receiving the vaccine, even if all are healthy and young, some serious

events can be expected within days or hours of vaccination by chance alone and unrelated to vaccination.

The most common side effects seen in studies with Gardasil (i.e. more than 1 patient in 10) were pyrexia, pain, erythema and swelling at the injection site. Gardasil should not be used in people who may be hypersensitive to the active substance or any of the other ingredients. If a patient shows signs of an allergy after a dose of Gardasil, she should not receive further doses of the vaccine. Vaccination should be postponed in patients who are ill with a high fever.

Fainting (or vasovagal syncope) and panic attacks, including mass episodes, can occur during, following, or even before, vaccination especially in adolescents and young adults. Syncope, sometimes associated with falling, has occurred after vaccination with Gardasil. Therefore, vaccinees should be carefully observed for an appropriate period of time after administration of Gardasil (see the Summary of Characteristics for further information). Faints or panic attacks occurring during or very shortly after vaccination are usually a psychogenic response to the needle injection and not a true side-effect of the vaccine.

Anaphylaxis is a very rare side-effect of most vaccines. The IMB wishes to remind healthcare professionals that, as with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a serious allergic reaction and possibly a rare anaphylactic event following the administration of the vaccine. An appropriate post-vaccination monitoring period should be observed in line with local guidance.

IMB Pharmacovigilance Strategy

Many adolescents will be immunised with Gardasil in Ireland over a relatively short period of time in the coming months. No vaccine is without side-effects, and adverse events/ reactions following immunisation with Gardasil will be closely monitored by the Irish Medicines Board. The IMB continuously monitors the safety of all vaccines and medicines used in Ireland, including Gardasil HPV Vaccine (as well as Cervarix HPV vaccine, which is not currently the HPV vaccine used in the routine immunisation programme). It is important to bear in mind that a report of a suspected adverse reaction does not necessarily mean that it has been caused by Gardasil. Reports may represent true adverse effects, or they may be due to underlying illness and therefore purely coincidental events that would also have occurred in the absence of vaccination. The IMB will monitor national experience with use of Gardasil, in the context of global safety data and will collaborate, as appropriate with EU and International counterparts in the evaluation of these data, communicating nationally, as necessary.

A significant volume of reporting of adverse events is often seen shortly after the introduction of a vaccine to a national immunisation campaign because of the increased exposure, higher degree of vigilance and limited national experience with the new product. Many of the reported events may be equally common in people of the same age who have not received the vaccine. Therefore, epidemiological methods are generally required to detect and investigate potential safety signals and regulatory mechanisms are in place across the EU to facilitate any necessary evaluation.

As part of the HPV vaccine pharmacovigilance strategy, at the start of the immunisation programme the IMB has written to healthcare professionals involved to encourage use of the national spontaneous reporting system to report suspected side effects. This system is also open to members of the public, who may wish to report their experience directly.

Adverse reactions may be reported using the *online Adverse Reaction Report* form. A downloadable version of the *Adverse Reaction Report form* is also available, which can be filled in manually and sent to the IMB by freepost.

If you have any queries in respect of adverse reaction reporting please contact: Pharmacovigilance Unit at imbpharmacovigilance@imb.ie