Health Canada Santé Canada

Date issued October 23, 2006

# NOTICE OF DECISION for GARDASIL™

On July 10, 2006, Health Canada issued a Notice of Compliance to Merck Frosst Canada Ltd. for the vaccine product Gardasil™.

Gardasil™ is a quadrivalent Human Papillomavirus (HPV) (Types, 6, 11, 16, 18) recombinant vaccine and an active immunizing agent. Gardasil™ contains as active ingredients, highly purified virus-like particles (VLPs) of the recombinant major capsid (L1) protein of HPV types 6, 11, 16, and 18. As the VLPs do not contain viral DNA, they cannot infect cells or reproduce. Data from pre-clinical studies suggest that the efficacy of L1 VLP vaccines is mediated by the development of humoral immune responses.

Gardasil™ is indicated in girls and women 9-26 years of age for the prevention of infection caused by the HPV (Types 6, 11, 16, and 18) and the following diseases associated with these HPV types: cervical cancer, vulvar and vaginal cancer, genital warts (condyloma acuminata), cervical adenocarcinoma *in situ* (AIS), cervical intraepithelial neoplasia (CIN) grades 1, 2 and 3, vulvar intraepithelial neoplasia (VIN) grades 2 and 3, and vaginal intraepithelial neoplasia (VaIN) grades 2 and 3.

Gardasil™ was reviewed under the Priority Review Policy as it offers a new prevention method of the indicated conditions that is expected to at least complement and augment the prevention of cervical cancer, through the existing screening program in Canada.

The market authorization was based on submitted data from quality control studies and a total of 10 pre-clinical studies and 12 clinical studies. The efficacy of Gardasil™ was assessed in 4 placebo-controlled, double-blind, randomized Phase II and III clinical studies. Gardasil™ was efficacious against HPV disease caused by each of the 4 HPV types contained in the vaccine. The efficacy of Gardasil™ in reducing the incidence of CIN (any grade, including CIN 2/3); AIS; genital warts; VIN (any grade); and VaIN (any grade) was demonstrated in a population consisting of individuals who received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, and were naïve (negative cervicovaginal specimens and seronegative) to the relevant HPV types (6, 11, 16, and 18) prior to the first dose and one month following the third dose.

Gardasil™ (quadrivalent human papillomavirus [types 6, 11, 16, 18] recombinant vaccine) is presented as a suspension for injection. Gardasil™ should be administered intramuscularly as three separate 0.5 mL-doses according to the schedule outlined in the dosing guidelines available in the Product Monograph.

Gardasil™ is contraindicated for patients who are hypersensitive to the active substance or to any of the excipients of the vaccine. For a complete listing, see the Dosage Forms, Composition and Packaging section of the Product Monograph. Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of Gardasil™ should not receive further doses. Gardasil™ should be administered under the conditions stated in the Product Monograph taking into consideration the potential risks associated with the administration of this drug product. Detailed conditions for the use of Gardasil™ are described in the Product Monograph.

Based on the Health Canada review of data on quality, safety, and effectiveness, Health Canada considers that the benefit/risk profile of Gardasil™ is favourable for the prevention of infection caused by the HPV (Types 6, 11, 16, and 18) and the following diseases associated with these HPV types: cervical cancer, vulvar and vaginal cancer, genital warts (condyloma acuminata), cervical adenocarcinoma *in situ* (AIS), cervical intraepithelial neoplasia (CIN) grades 1, 2, and 3, vulvar intraepithelial neoplasia (VIN) grades 2 and 3, and vaginal intraepithelial neoplasia (VaIN) grades 2 and 3 in girls and women 9-26 years of age.



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