



New Drug Focus

Gardasil™ – Quadrivalent HPV vaccine

Gardasil™ is a new vaccine used to prevent cervical cancer and genital warts caused by human papillomavirus (HPV) types 6, 11, 16 and 18. The vaccine targets the HPV strains that are associated with 70% of cervical cancers (i.e. HPV 16 and 18) and with 90% of genital warts (i.e. HPV 6 and 11). While HPV 6 and 11 are not associated with cervical cancer, they can cause abnormal Pap smears.

Worldwide, cervical cancer is the second most common cancer in women. Almost 80% of cervical cancer cases occur in the developing world, largely because these women are less likely to undergo regular cervical cancer screening with a Pap test, a simple diagnostic test that detects abnormal or cancerous cervical cells.

Approved indications

Children from 9 to 17 years of age and women from 18 to 26 years of age are candidates for HPV vaccination. This quadrivalent vaccine is indicated for:

- The prevention of cervical, vulvar and vaginal cancer
- The prevention of cervical, vulvar and vaginal intraepithelial neoplasia grades 2 and 3
- The prevention of cervical intraepithelial neoplasia grade 1
- The prevention of genital warts
- The prevention of HPV infection with HPV 6, 11, 16 and 18

Mode of action

The vaccine contains virus-like particles, which are proteins that resemble wild-type HPV 6, 11, 16 and 18. The virus-like particles do not contain any viral DNA and therefore cannot infect cells or reproduce.

The administration of the vaccine induces the formation of antipapillomavirus antibodies to the strains contained in the vaccine, resulting in protection against infection by HPV 6, 11, 16 and 18.

Dosage

The vaccine is administered intramuscularly in the deltoid region of the upper arm or in the anterolateral area of the thigh in a three-dose schedule as follows:

- 1st dose at the elected date
- 2nd dose – Two months after the first dose

- 3rd dose – Six months after the first dose
- The duration of the efficacy of the vaccine and whether boosters are needed are not known.

Evidence of efficacy

The Phase III studies (FUTURE I and FUTURE II) evaluated the efficacy of Gardasil™ in 20 541 women between the ages of 16 and 26 years. The results of the FUTURE I study show that the vaccine is highly effective in preventing clinical disease, including intraepithelial neoplasia of the cervix, vagina and vulva and anogenital warts associated with HPV 6, 11, 16 and 18. There appears to be no interference among the four HPV types covered by the vaccine, since 100% HPV-type efficacy was observed.

Precautions

• General

The vaccine is contraindicated for use in patients with a hypersensitivity to the active ingredients or to any excipients of the vaccine. The vaccine should be used with caution in individuals with thrombocytopenia or any coagulation disorders because bleeding may occur following intramuscular administration.

The safety and efficacy of the vaccine have not been evaluated in children under 9 years of age nor in adults over the age of 26 years.

The safety, efficacy and immunogenicity of the vaccine have not been evaluated in HIV-infected individuals. Impaired immunity, whether due to immunosuppressive therapy, a genetic defect or HIV infection may cause a reduced antibody response to immunisation.

• Pregnancy and lactation

There are no adequate studies in pregnant women. The vaccine is not recommended for use during pregnancy and women found to be pregnant before completion of the immunisation schedule should defer the completion of the vaccine series until after delivery. The vaccine may be administered to lactating women.

Major adverse effects

The vaccine has demonstrated a favourable safety profile when compared with placebo. More common adverse effects vs placebo include redness, pain and swelling at the injection site, pyrexia, pruritis and bleeding.

Bronchospasm is a rare serious adverse event. As with all vaccines, appropriate medical treatment should be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

Drug interactions

Although there is no data, individuals receiving concomitant therapy with potent immunosuppressants (e.g. high doses of systemic corticosteroids, antimetabolites, alkylating agents or cytotoxic agents) may not respond optimally to immunisation.

Single Exit Price

Gardasil™ R770.00 (EXCL VAT)/dose
Manufactured by MSD (Pty) Ltd.

Patient information

It is important to tell patients that 30% of cervical cancers are caused by HPV types not present in the vaccine. In other words, a woman may be vaccinated according to the recommended schedule and still become infected with an HPV type not contained in the vaccine. Women infected with one or more vaccine HPV types before vaccination would be protected against disease caused by the other vaccine HPV types.

Women are advised to have regular Pap smears, regardless of whether they have been vaccinated or not. Lack of screening is a major contributing factor to cervical cancer mortality.

Conclusion

The HPV vaccine does not completely eliminate cervical cancer risk. However, when given to women not previously infected with HPV types 6, 11, 16 and 18, it is highly effective in preventing infection. □

References:

1. Gardasil Package Insert.
2. Gardasil Patient Information Leaflet.
3. Garland SM, Hernandez-Avila M, Wheeler CM, *et al.* Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *New Engl J Med* 2007;356(19):1928-1943.
4. www.medscape.com

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