Pharmacotherapeutic report on the herpes zoster vaccine (Zostavax®) for the prevention of herpes zoster and herpes zoster-related post-herpetic neuralgia

Recommendation by CVZ[1] dated 24 February 2014, based on Evaluation by the WAR (Scientific Advisory Committee).

The National Health Care Institute's Scientific Advisory Committee (WAR) has approved a pharmacotherapeutic report for the herpes zoster vaccine (Zostavax®).
Assessment of the therapeutic value of this drug is based on the claim of the Market Authorisation Holder, which is limited to adults aged 70 years or older. Comparison took place with placebo. The WAR reached the follow conclusions:
Zostavax® has an added therapeutic value in comparison with placebo for the prevention of herpes zoster (HZ) and herpes zoster-related post-herpetic neuralgia (PHN) in immunocompetent adults aged 70 years or older.

Medicine. Zostavax® (live, attenuated vaccine with the varicella-zoster virus), powder and solution for suspension for injection.

Registered indication. "For the prevention of herpes zoster (HZ, shingles) and herpes zoster-related post-herpetic neuralgia (PHN) in individuals 50 years of age or older".

Posology. A single dose (0.65 ml) injected subcutaneously, preferably in the deltoid region. A dose of 0.65 ml contains no less than 19,400 plaque-forming units of the varicella zoster virus (Oka/Merck-strain).

Mechanism of action. HZ develops due to reactivation of the varicella zoster virus (VZV). Primary infection with VZV manifests as chickenpox. After recovery the virus remains latent in the sensory ganglia. As people age their (virus-specific) immunity is reduced so that the virus can become active again. The herpes zoster vaccine reinforces VZV-specific immunity and thus represses reactivation of the virus. When HZ does not develop, PHN will not occur either as it is a consequence of HZ.

Specific details.

1. Zostavax® is intended for the prevention of shingles among adults from the age of 50 years. In principle, the intervention is not based on a currently existing medical need of the vaccinee.
2. The initial registration of Zostavax® was for a formulation that had to be stored and transported below zero degree centigrade. Most clinical studies were carried out with this frozen formulation of Zostavax®. The currently registered presentation form of Zostavax® is a formulation that remains stable at refrigeration temperatures (storage and transport at 2-8^{o} C). The efficacy of this refrigerated formulation has been demonstrated via a bridging study, whereby the VZV antibody response of both formulations were compared.

[1]N.B. On 1 April 2014 CVZ (Health Care Insurance Board) became *Zorginstituut Nederland* (National Health Care Institute).

Summary of therapeutic value

Intended effects. Vaccination of immunocompetent individuals aged 70 years or older with the herpes zoster vaccine leads to a reduced risk of developing HZ and also, therefore, the PHN that may follow in its wake. The favourable effects of this vaccine are related to an individual's ability to develop an immune response upon vaccination. Ageing or an immunocompromised status can lead to a reduced immune response. Overall vaccine efficacy for preventing both disorders is 38% and 47% respectively in comparison with placebo, with favourable results in younger cohorts and less favourable ones in older cohorts. No data have been published on the effect of the herpes zoster vaccine on pain due to HZ in individuals aged 70 years or older. The herpes zoster vaccine does not affect the quality of life of an individual who has developed HZ. Although research is in progress, no clinical studies have been published on the effects of this drug on individuals with immunodeficiency.

Unintended effects. Most of the side effects reported with the herpes zoster vaccine are local reactions at the vaccination injection site. The responses, which are generally mild, occur more frequently after administering the vaccine in comparison with placebo. One or more severe side effects has been seen in 1.66% of the individuals who received the vaccine. This percentage does not differ significantly from the control group (1.78%).

Experience. The herpes zoster vaccine has been registered in Europe since 2006. Sufficient experience has been obtained with this drug in adults aged 70 years or older.

Applicability. The herpes zoster vaccine is contraindicated in, among others, individuals with an immunodeficient state due to illness or treatment that suppresses the immune system. This vaccine may not be administered simultaneously with the 23-valent polysaccharide pneumococcal vaccine because this leads to decreased immunogenicity of the herpes zoster vaccine. It is possible to administer inactivated influenza vaccine simultaneously, as long as both injections are given separately and in different sites on the body. No data are available on the simultaneous administration of other vaccinations such as travellers' vaccinations.

Ease of use. Herpes zoster vaccine is injected once only subcutaneously. It is not known whether a booster injection is required and if so, when.

Final conclusion on therapeutic value.

The herpes zoster vaccine has an added therapeutic value in comparison with placebo for the prevention of herpes zoster (shingles) and post-herpetic neuralgia in immunocompetent adults aged 70 years or older. The vaccine's efficacy has been demonstrated for the prevention of HZ and PHN. The risk of developing a serious side effect does not differ significantly between people who have been vaccinated with the herpes zoster vaccine in comparison with placebo. This vaccine does not affect the quality of life of a person who develops HZ. No data are available on the effect of the herpes zoster vaccine on pain due to HZ in individuals aged ≥70 years.

*The original text of this **WAR-Report** of the National Health Care Institute was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of the National Health Care Institute's WAR-Report.*
Furthermore, the National Health Care Institute points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.