HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASES
New medicinal product
September 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

GARDASIL 9, 9-valent human papillomavirus vaccine

Substantial clinical benefit in the prevention of precancerous and cancerous anogenital lesions, but no clinical benefit demonstrated compared with GARDASIL

Main points

- GARDASIL 9 has Marketing Authorisation in active immunisation against diseases related to certain human papillomaviruses (HPV): genital warts and precancerous and cancerous lesions of the cervix, vulva, vagina and anus.
- Its composition includes five additional types of HPV (HPV 31, 33, 45, 52 and 58) compared to GARDASIL, which it is intended to replace.
- It induces an immune response comparable to that of GARDASIL as far as the primary HPV pathogens (HPV 6, 11, 16 and 18) and its efficacy in terms of prevention of cancers remains to be demonstrated.

Therapeutic use

- Anti-HPV vaccination is recommended:
  - in girls aged 11 to 14 years, and as catch-up vaccination up to 19 years of age inclusive,
  - in men who have sex with men (MSM) up to 26 years of age,
  - in immunosuppressed persons up to 19 years of age.
- Vaccination coverage is insufficient in France. Therefore, it must be accompanied by broad and well-explained information for health professionals and the public about HPV diseases, vaccines and the effectiveness of vaccination.
- This vaccination is in addition to screening by Pap smear in the prevention of precancerous and cancerous lesions of the cervix.
- **Role of the medicinal product in the therapeutic strategy**

  GARDASIL 9 is recommended for initiating vaccination in eligible populations:
  - according to the 2-dose regimen in girls aged 11 to 14 years inclusive who have not previously been vaccinated,
  - according to the 3-dose regimen in girls aged 15 to 19 years inclusive, MSM until age 26 years and immunosuppressed persons until age 19 years.

  As no interchangeability data is available, it is recommended that the entire vaccination regimen be done with the same vaccine (CERVARIX, GARDASIL or GARDASIL 9).

Clinical data

- For HPV 6, 11, 16 and 18 already included in GARDASIL (responsible for most genital warts and 70 to 80% of anogenital cancers), the immune response induced by GARDASIL 9 was non-inferior to the immune response induced by GARDASIL.
- For the additional HPV 31, 33, 45, 52 and 58 (involved in 5 to 20% of anogenital cancers), the vaccine efficacy of GARDASIL 9 was 97.4% (95% CI [85.0; 99.9]), i.e. an absolute reduction of 0.2 per 100 person-years for high-grade lesions (previously called CIN 2/3) in girls and women aged 16 to 26 years not infected by HPV during vaccination. No benefit was demonstrated in women already infected by HPV during the vaccination.
- The safety profile of GARDASIL 9 is similar to that of GARDASIL despite a higher frequency of local reactions. The most common adverse effects are comparable to those of vaccines commonly used between 9 and 26 years of age; most of the reactions were benign and temporary, such as: pain at the injection site (83%), headache (13%), fever (6%) and nausea (3%).

- In addition, an increased risk of Guillain-Barré syndrome of approximately 1 to 2 cases per 100,000 young women vaccinated with GARDASIL or CERVARIX was observed in an epidemiological study conducted by the French National Agency for Medicines and Health Products Safety (ANSM) and National Salaried Workers' Health Insurance Fund (CNAMTS).
- The currently available data do not provide answers to questions concerning:
  - the interchangeability of GARDASIL 9 with other HPV vaccines (bivalent or quadrivalent),
  - the potential risk of selection of replacement HPV genotypes following introduction of GARDASIL 9,
  - the maintenance of the vaccine effect with the 2-dose regimen,
  - the levels of vaccination coverage that will be obtained in the recommended populations in France,
  - the efficacy in terms of prevention of cancers, as for GARDASIL and CERVARIX vaccines.

Benefit of the medicinal product

- The actual benefit* of GARDASIL 9 is substantial in the recommended populations.
- GARDASIL 9 does not provide clinical added value** (CAV V) by comparison with GARDASIL in the prevention of precancerous and cancerous anogenital lesions related to certain HPV.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 13 September 2017 (CT-15867) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".