HAUTE AUTORITÉ DE SANTÉ

INFECTIOLOGY
New medicinal product
October 2014

BREIF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ZOSTAVAX, live attenuated shingles (herpes zoster) vaccine

Minor therapeutic improvement in the prevention of herpes zoster and postherpetic neuralgia in the populations recommended by the French High Council for Public Health

Main points

- ZOSTAVAX is a live attenuated vaccine with Marketing Authorisation in the prevention of herpes zoster and postherpetic neuralgia in adults age 50 and over.
- Its efficacy is modest on the incidence of herpes zoster and its protection decreases with the vaccination age and over time.
- This vaccine must be used according to the recommendations of the French High Council for Public Health (HCSP), i.e. in non-immunocompromised patients 65 to 74 years old.

Therapeutic use

- According to the French High Council for Public Health, ZOSTAVAX vaccination is recommended in adults 65 to 74 years old with a single-dose vaccination schedule. During the first year following inclusion of the vaccine in the vaccination calendar, individuals 75 to 79 years of age might also be vaccinated. (http://www.hcsp.fr/explore.cgi/avisrapportsdomaine?*clefr*=390HCSP)
- ZOSTAVAX is contraindicated in immunocompromised individuals.
- The need for a booster dose is currently unknown.
- **Role of the medicinal product in therapeutic strategy**
  ZOSTAVAX is recommended for prevention of herpes zoster and postherpetic neuralgia (PHN) in adults 65 to 74 years old, non immunocompromised.

Clinical data

- A randomised, placebo-controlled study conducted in adults above age 60 showed:
  - an efficacy of 61.1% [95% CI = 51.1; 69.1] on the HZ-associated pain severity score for, the composite primary endpoint taking into account the incidence, severity and duration of pain associated with herpes zoster as well as the discomfort related to herpes zoster.
  - a decrease in the incidence of herpes zoster (secondary endpoint) of 51.3% [95% CI = 44.2; 57.6], corresponding to an absolute reduction of 5.7 cases of herpes zoster per 1000 person-years, decreasing as vaccination age increase (reduction of the incidence of herpes zoster by 63.9% among 60-69 year-olds and 37.6% in those over 70 years).
  - a decrease in the incidence of PHN:
    - among all subjects (co-primary endpoint) of 66.5% [95% CI = 47.5; 79.2] corresponding to an absolute reduction of PHN of 0.92 cases per 1000 person-years.
    - in patients who have had herpes zoster, prerequisite for the occurence of PHN (FDA post-hoc analysis), the reduction of PHN incidence was of 39% [95% CI = 7; 59].
- Observational studies conducted retrospectively from databases in the United States found similar results on the incidence of shingles.
- In open-label follow-up studies, vaccine protection seems to wane over time, becoming uncertain for the prevention of herpes zoster beyond 5 years from vaccination. There is therefore a potential risk of postponing the occurrence of herpes zoster at a more advanced aged, in the most vulnerable individuals for whom the disease complications are more frequent and more severe.

- The need for boosters to provide durable individual protection has not been established.Safety data show an elevated frequency (≥ 10%) of local reactions (pain, redness, swelling, itching).

Benefit of the medicinal product

- In view of:
  - the modest efficacy on the incidence of herpes zoster in the populations recommended by the HCSP,
  - the decrease in vaccine protection with age and over time,
  - the contraindication of vaccination in immunocompromised subjects,

  the actual benefit* of ZOSTAVAX is moderate in the prevention of herpes zoster and PHN in the populations recommended by the HCSP.
- ZOSTAVAX provides a minor clinical added value** (CAV IV) in the prevention of herpes zoster in the populations recommended by the HCSP.
- 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 15 October 2014 (CT-13478) and is available on **www.has-sante.fr**

[i] * 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 by the National Health Insurance.

** 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".