

PUBLIC SUMMARY DOCUMENT

Product: Human Papillomavirus (Types 16 and 18) recombinant, AS04 adjuvanted vaccine, injection, 0.5 ml vial and pre-filled syringe, Cervarix[®]

Sponsor: GlaxoSmithKline Australia Pty Ltd

Date of PBAC Consideration: November 2007

1. Purpose of Application

The re-submission sought to address the main areas of uncertainty considered by the PBAC at the July 2007 meeting. A revised economic model was presented that incorporated a revised price compared to the previous submission for consideration.

2. Background

At its July 2007 meeting, the PBAC considered a submission seeking Cervarix listing on the National Immunisation Program (NIP) for the prophylactic vaccination of 12 and 13 year old girls (with a two-year catch up program for girls and women aged 13-26) against cervical cancer and precancerous lesions associated with HPV-16 and HPV-18. The PBAC rejected the application on the basis of uncertain cost-effectiveness against the comparator, Gardasil[®]. (See also *Public Summary Document for July 2007*)

3. Registration Status

Cervarix has been registered with the TGA since 18 May 2007. Cervarix is indicated in females from 10 to 45 years for the prevention of cervical cancer by protecting against incident and persistent infections, cytological abnormalities including atypical squamous cells of undetermined significance (ASC-US) and cervical intraepithelial neoplasia (CIN), CIN 1 and pre-cancerous lesions (CIN 2 and CIN 3) caused by HPV types 16 and 18. Immunogenicity studies have been conducted in females aged 10 to 14 years and 26 to 45 years to link efficacy in females aged 15 to 25 years to other populations.

4. Listing Requested and PBAC's View

The requested NIP indication was:

Prophylactic vaccination of 12 and 13 year old girls (with a two-year catch up program for girls and women aged 13-26) against cervical cancer and precancerous lesions associated with HPV-16 and HPV-18.

The PBAC had no objections to the requested wording of the restriction.

5. Clinical Place for the Proposed Therapy

Infection with human papillomavirus (HPV) has been clearly established as the central cause of cervical cancer. In Australia, HPV-16 and HPV-18 account for approximately 70% of all cervical cancers and up to 50% of high-grade pre-cancerous lesions. Therefore, an effective HPV-16/18 vaccine is expected to represent an important preventative, primary health care intervention against cervical cancer and pre-cancerous cervical lesions.

Cervarix is a human papillomavirus vaccine that protects against infection caused by HPV-types 16 and 18.

6. Comparator

There was no change to the comparator nominated previously.

7. Clinical Trials

As reported in the July 2007 Public Summary Document.

8. Results of Trials

As reported in the July 2007 Public Summary Document.

9. Clinical Claim

The re-submission was based on the conservative assumption that Cervarix is equivalent to Gardasil with respect to efficacy against cervical cancer caused by HPV-16/18 and that Gardasil offers the additional health benefit of protection against genital warts when compared to Cervarix. (*see Sponsor comments*)

10. Economic Analysis

The submission presented a revised economic model to address one of the key factors that the PBAC considered at the July 2007 meeting, that is, the value of the health loss associated with the lack of coverage against genital warts if Cervarix rather than Gardasil is used. Hence, the re-submission proposed a different price compared to the previous submission. This resulted in a cost saving in the range \$45,000 - \$75,000 per QALY foregone.

11. Estimated PBS Usage and Financial Implications

No further PBS usage or financial analyses were included in the submission. The sponsor has indicated that it is willing to develop an appropriate risk sharing arrangement to address any uncertainties surrounding the inclusion of Cervarix on the NIP.

12. Recommendation and Reasons

The PBAC recalled that it had previously rejected a submission to list Cervarix on the NIP on the basis of uncertain cost-effectiveness against the comparator, Gardasil[®], noting the following:

- Cervarix was as effective as Gardasil in protection against the cancer-causing HPV types 16 and 18;
- There was uncertainty about the comparative efficacy of the two vaccines in terms of cross protection against other cancer-causing HPV types; and
- Gardasil offered protection against genital warts.

The PBAC considered that there continued to be uncertainty about the comparative efficacy of the two vaccines in terms of cross protection against other cancer-causing HPV types.

The submission provided a revised estimate of the incremental benefit that Gardasil offers over Cervarix through genital warts protection and the value of the health loss associated with the lack of coverage against genital warts if Cervarix rather than Gardasil is used.

The PBAC accepted that most of the assumptions in the economic model favoured Gardasil. The exception to this was the assumption of waning of Gardasil efficacy against genital warts. There were also residual concerns about equity, because individual patients are not offered a choice between vaccines, since decisions are made at the State level. However, given that all other assumptions did not favour Cervarix and there is a recognised need for more than one vaccine to be available in the event of supply shortages, the PBAC was prepared to accept that Cervarix is acceptably cost-effective at the new price and thus recommended the inclusion of Cervarix in the National Immunisation Program.

The PBAC also recommended that GSK provide the same contribution towards the national cervical screening program as has the sponsor of Gardasil and that it maintain a register of persons vaccinated. Further, in any risk-sharing agreement, the same conditions should apply concerning the possibility of a requirement for re-vaccination if the efficacy of the vaccine should wane.

Recommendation

List on the NIP for the prophylaxis against HPV-16 and HPV-18 of 12 and 13 year old girls (with a two-year catch up program for girls and women aged 13-26), with vaccination at 0, 1 month and 6 months.

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

GSK believes the PBAC has significantly undervalued the evidence of some cross-protection by *Cervarix* against infection caused by HPV-31 and HPV-45, and significantly overvalued the clinical and economic importance of the protection offered by *Gardasil* against genital warts.