PUBLIC SUMMARY DOCUMENT

Product: Rotavirus vaccine, live, oral liquid, pentavalent, 2 mL unit dose RotaTeq®

Sponsor: CSL Ltd

Date of PBAC Consideration: November 2006

1. Purpose of Application

The resubmission sought to address the main areas of uncertainty raised by the PBAC at the July 2006 meeting.

The resubmission requested listing on the National Immunisation Program (NIP) for the vaccination of infants at 2, 4 and 6 months of age to prevent rotavirus gastroenteritis (RVGE), as in the first submission (July 2006).

2. Background

At the July 2006 meeting, the PBAC rejected the submission for this vaccine because of uncertain cost-effectiveness at the price requested. There were a number of uncertainties over the modelled economic evaluation. Of particular concern to the PBAC was the treatment of quality adjusted life year (QALY) gains. The second uncertainty identified in the cost-effectiveness analysis based on QALYs was the impact of the death rates from rotavirus on the results of the modelled economic evaluation. The third uncertainty identified by the PBAC was treatment of production gains. Fourthly, the PBAC also considered that the cost of administration of an oral vaccine should have been included in the economic model. The PBAC also noted that the impact of hospital acquired (nosocomial) rotavirus infections had not been included in the economic evaluation.

3. Registration Status

RotaTeq vaccine is registered for the prevention of rotavirus gastroenteritis.

4. Listing Requested and PBAC's View

National Immunisation Schedule

The vaccination of all infants at 2, 4, and 6 months of age to prevent rotavirus gastroenteritis.

See Recommendation and Reasons for the PBAC's view.

5. Clinical Place for the Proposed Therapy

Vaccination is proposed to reduce/prevent the incidence of rotavirus gastroenteritis in infants and children. Rotavirus is very common in human and animal hosts and is the most common cause of severe gastroenteritis in infants and young children and a major cause of hospitalisation and morbidity in developed countries.

6. Comparator

The July 2006 submission nominated standard medical management without rotavirus vaccination. The PBAC agreed that this was the appropriate comparator.

7. Clinical Trials

The submission did not present any new clinical trials but presented two systematic reviews of studies on nosocomial infections, and a prospective study examining nosocomial rotavirus infection in an Australian hospital.

These reviews had been published at the time of submission as follows:

Trial/First author	Publication title	Publication citation
Fischer TK et al (2004)	Rotavirus vaccines and the prevention of hospital-acquired diarrhea in children.	Vaccine, 22S: S49-54
Gleizes O et al (2006)	Nosocomial Rotavirus Infection in European Countries.	Pediatric Infectious Disease Journal, 25(1): S12-21
Ringenbergs ML et al (1989)	Prospective study of nosocomial rotavirus infection in a paediatric hospital.	Aust. Paediatr. J., 25: 156-160

The resubmission also presented an unpublished manuscript which analysed rotavirus-related admission data from the Australian Institute of Health and Welfare National Hospital Morbidity Database for 2000-01 and 2001-02.

8. Results of Trials

No new data were presented. The results of the trials had previously been described in the July 2006 Public Summary (PSD).

9. Clinical Claim

As previously, the submission described RotaTeq as having significant advantages in effectiveness over standard medical management and having similar or less toxicity.

10. Economic Analysis

A revised modelled economic evaluation was presented using altered key variables as follows:

- Reduction in the cost per dose of RotaTeq
- Impact of death rates.
- Treatment of production gains (ie work loss costs).
- Cost of administration.
- Impact of nosocomial infections.

All other variables are the same as the original submission.

The cost (excluding work loss costs) per QALY gained in the revised evaluation was <$15,000, compared to $45,000 – $75,000 in the original submission.

11. Estimated PBS Usage and Financial Implications

The revised estimated net cost to the NIP was in the range $30 – 60 million in year 4.

12. Recommendation and Reasons

The PBAC recommended inclusion of RotaTeq on the NIP for the indication requested by the sponsor on the basis of acceptable cost-effectiveness. RotaTeq was considered to be of similar safety and efficacy to Rotarix (determined at the July 2006 meeting).

The PBAC noted the following matters were outstanding from that meeting:

- The sponsor's treatment of QALY gains.
- The impact of the death rates applied in the model of the cost-effectiveness results.
- Inclusion of production gains.
- Inclusion of cost of administration of an oral vaccination.
- Whether the impact of nosocomial infections should be included in the model – this latter factor was raised by the PBAC as a (then un-estimated but claimed) benefit of the vaccine, which required more accurate estimation.

The PBAC noted in its analysis of the resubmission that the sponsor's request had remained unchanged (ie funding for all children under the NIP at 2, 4 and 6 months of age). The key changes to the submission are:

- The requested price for a dose of RotaTeq has been reduced.
- A new estimate of the death rate has been included.
- Production gains have been excluded from the base case.
- A detailed assessment of the possible costs of administration has been included.
- The costs of nosocomial infection have been included.

The PBAC still considered the treatment of QALY gains to be problematic as to whether it is reasonable to assume that there is a QALY gain from avoidance of rotavirus (ie a gain in quality of life (QOL) that is measurable on a scale that trades QOL against survival), and whether the QALY weights and resultant QALYs are reasonable.

For this submission the estimates of QALY gains were obtained from application of the HUI2 in an appropriate population. While there may continue to be disagreement about whether it is appropriate to attempt to elicit QALY impacts for rotavirus, the method can be argued to be relatively conservative – particularly given that it uses a general practice population and applies the QALY weight only to the symptomatic days. Even if it is not appropriate to use a QALY metric in this case, it might be reasonably argued that this measure might be a reasonable proxy for the welfare impact (QOL) of rotavirus. It is unlikely that any more valid estimate will be available from an alternative method.

The PBAC was satisfied with the sponsor's treatment of the estimate of the death rate, the cost of administration of an oral vaccine, and how nosocomial infections were estimated and costed. Listing was recommended on the basis of acceptable cost-effectiveness versus placebo.

Recommendation

PENTAVALENT HUMAN-BOVINE ROTAVIRUS ORAL VACCINE, oral, 2mL

National Immunisation Schedule

Vaccination of all infants at 2, 4 and 6 months of age against rotavirus strains G1, G2, G3, G4 and P1

Pack size: 1

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

CSL is pleased with the decision to recommend inclusion of RotaTeq on the NIP for all children at 2, 4 and 6 months of age. The inclusion of RotaTeq on the NIP will lead to a major reduction in hospitalisation and general practitioner visits for gastroenteritis in Australian children, and reduction in associated distress to those children and their parents. In addition to reduction in health care usage, RotaTeq will lead to significant reductions in work loss for parents having to care for young children with rotavirus gastroenteritis.

However, despite the positive decision CSL has remaining concerns that the PBAC still considers the treatment of quality of life gains with RotaTeq 'to be problematic', and that work loss savings will not be accepted in the base-case of the economic analysis. CSL will continue to work with the PBAC and Government on these issues.