OPINION ON MEDICINAL PRODUCTS

Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine, (adsorbed, reduced antigen content)

REPEVAX,

suspension for injection in prefilled syringe

Amendment of terms of inclusion following update of vaccination guidelines

Adopted by the Transparency Committee on 23 November 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement for passive protection against pertussis during early childhood after maternal immunisation during pregnancy, according to the HAS guidelines in force of 7 April 2022.

Therapeutic improvement?

Therapeutic improvement in the care pathway.

Role in therapeutic strategy?

In April 2022, HAS drafted pertussis vaccination recommendations for pregnant women, updating the role of the BOOSTRIXTETRA and REPEVAX vaccines in the prevention strategy.

According to the vaccination guidelines adopted by the HAS Board on 07/04/2022, “HAS recommends pertussis vaccination for pregnant women from the second trimester of gestation, preferably the period between 20 and 36 amenorrhoea weeks (AW), in order to increase passive transplacental transfer of maternal antibodies and ensure optimal protection for the newborn. Vaccination during pregnancy may be performed with a trivalent vaccine (dTca) or tetravalent vaccine (dTcaP) depending on availability.

HAS recommends that pertussis vaccination be administered for each pregnancy. A woman who has received a pertussis vaccine before her pregnancy must also be vaccinated during the current pregnancy, in order to ensure that enough antibodies are transferred through the placenta to protect the future newborn. In any case, a minimum interval of one month must be observed with respect to the most recent dTP vaccine.

Failing vaccination of the pregnant woman during pregnancy, vaccination is recommended:

- for the mother in the immediate post-partum period, before she is discharged from the maternity hospital, even if she is breastfeeding, in accordance with the current cocooning strategy;
- for the newborn’s relatives (parents, siblings, grandparents, and other people liable to be in long-term close contact with the future infant for the first six months of their life) no later than at the time of the infant’s birth.

HAS specifies that, when the mother has been vaccinated during pregnancy, and at least one month has elapsed between vaccination and delivery, it is no longer necessary to vaccinate the infant’s close relatives.

However, HAS recommends that pertussis vaccination be preferably performed during pregnancy; this strategy has demonstrated a superior real-life vaccination efficacy in protecting infants in the first months of their lives, and while awaiting their own vaccination. HAS notes that the vaccination of pregnant women against pertussis may be administered at the same time as seasonal influenza and/or COVID-19 vaccination (however, while pertussis vaccination should preferentially be administered during the second or third trimester of gestation, COVID-19 and influenza vaccination should be administered as early as possible during pregnancy).

HAS stresses that infants’ vaccination schedules must be observed in accordance with the guidelines in force, whether the mother has been vaccinated during pregnancy or not.”

Role of the medicinal product

Erreur ! Source du renvoi introuvable.

Special recommendations

➔ **Special requests inherent to funding**

The Committee insists that communication be targeted at pregnant women and healthcare professionals with vaccination expertise, in order to increase pertussis vaccination uptake through the passive protection strategy based on immunisation during pregnancy.

The Committee supports the request expressed in the HAS vaccination guidelines of April 2022 that pertussis vaccines be made available in maternity hospitals and other care facilities providing care for pregnant women, for administration to the pregnant woman during a regulatory pregnancy check-up.

➔ Other requests

The Committee regrets the lack of availability to date of a monovalent acellular pertussis vaccine, its preferred pharmaceutical dosage form, as previously stated in its inclusion opinion for REPEVAX.

Committee's conclusions

Actual Clinical Benefit

- ➔ Pertussis is a highly contagious respiratory tract infection. It causes frequent and prolonged coughing fits. Pertussis infection among younger infants is severe, or even fatal.
- ➔ The proprietary medicinal product REPEVAX (dTcaP vaccine) is a preventive medicinal product.
- ➔ The efficacy (immunogenicity)/adverse effect ratio is significant.
- ➔ A directly comparable alternative vaccination combining the same components (BOOSTRIXTETRA) is available.
- ➔ REPEVAX (dTcaP vaccine) may be used according to its marketing authorisation within the scope of the vaccination guidelines in force.

➔ Public health benefit

Considering:

- the severity of pertussis infection in infants, including more than 90% deaths occurring during the first six months of life. The average number of annual deaths attributable to pertussis is estimated at 2.6;
- the public health objective of lowering morbidity and mortality from this infection;
- that vaccination is the most effective prevention tool against pertussis;
- the medical need to expand the range of pertussis vaccines available;
- an expected impact of the proprietary medicinal product REPEVAX on lowering the incidence of pertussis infections and on associated morbidity-mortality in view of the immunogenicity and efficacy data available, and a reassuring safety profile in pregnant women, foetuses, and newborns;
- an expected impact of vaccination on the delivery of care (reduction of hospital admissions);

REPEVAX (dTcaP vaccines), int he same way as the tetravalent vaccine BOOSTRIXTETRA is likely to have an additional public health impact for passive protection against pertussis in early childhood after maternal immunisation during pregnancy.

Considering all of these elements, the Committee deems that the actual clinical benefit of REPEVAX (dTcaP vaccine) remains significant for passive protection against pertussis in early childhood after maternal immunisation during pregnancy, according to the HAS guidelines in force of 7 April 2022.

The Committee approves the continued inclusion of REPEVAX (dTcaP vaccine) in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for passive protection against pertussis in early childhood after maternal immunisation during pregnancy, according to the HAS guidelines in force of 7 April 2022, and at authorised dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- **the insufficiently met medical need in the protection of newborns and infants in the first three months of their lives against pertussis and its complications,**
- **the immune response induced by REPEVAX (dTcaP vaccine) in pregnant women, providing their infant with immunogenicity through transplacental transfer of pertussis antibodies for at least two months after birth,**
- **a real-life efficacy demonstrating an impact on lowering the incidence of pertussis among infants under 3 months of age, compared to infants of unvaccinated mothers (OR = 0.22, $CI_{95\%}$ = [0.14; 0.33]), and reducing hospital admissions associated with pertussis (direct estimations between 58% and 84%) and on the mortality attributable to pertussis (approximately 95%; $CI_{95\%}$ = [79; 100] in England and Wales) among infants under 3 months of age,**
- **the favourable safety profile in pregnant women, foetuses or newborns, without an increased risk of adverse events,**

the Committee deems that REPEVAX (dTcaP vaccine), provides moderate clinical added value (CAV III) in the same way as the tetravalent vaccine BOOSTRIXTETRA, for passive protection against pertussis in early childhood after maternal immunisation during pregnancy.