HAUTE AUTORITÉ DE SANTÉ

INFECTIOLOGY
New medicinal product
April 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ROTARIX and ROTATEQ, rotavirus vaccines

Insufficient actual benefit in the prevention of gastroenteritis due to rotavirus infection

Main points

- ROTARIX and ROTATEQ are live attenuated oral vaccines with Marketing Authorisation since 2006 in the prevention of acute gastroenteritis due to rotavirus infection (RV-AGE) in infants.
- The efficacy of these vaccines is high, but the most recent safety data confirm an increased risk of acute intussusception (AI) estimated at about 6 additional cases per 100,000 vaccinated individuals.
- In view of the risk of AI and given the epidemiology of RV-AGE in France, rotavirus vaccination is not expected to impact on public health if vaccine coverage is low.

Therapeutic use

- According to the opinion of the French High Council for Public Health (HCSP) of 29 November 2013, vaccination against rotavirus infections is recommended in babies under 6 months in a two-dose vaccination schedule (at age 2 and 3 months) for the vaccine ROTARIX and a three-dose schedule (at age 2 and 3 months) for the vaccine ROTATEQ. The HCSP states that this strategy is recommended only if the price of the vaccines is reflected in an acceptable cost/benefit relationship.
(http://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=405)
- Vaccination is contraindicated primarily in babies with:
  - known or suspected immunodeficiency;
  - congenital malformation of the gastrointestinal tract that would predispose for intussusception or a history of intussusception.

Role of the medicinal product in the therapeutic strategy

The prevention of gastroenteritis in infants is based on hygiene measures (hand washing, cleaning of surfaces) and breastfeeding. Vaccination is the sole available strategy over and above these measures in the prevention of RV-AGE. In France there are two available vaccines in this indication (ROTARIX since May 2006 and ROTATEQ since January 2007). This vaccination is not expected to benefit public health.

Clinical data

- The clinical studies have shown a vaccine efficacy of:
  - 87.1% (95% CI [79.6; 92.1]; $p < 0.001$), i.e. an absolute reduction of 131.7 cases per 1000 person-years for RV-AGE and 85% (RR = 0.15; 95% CI [0.12; 0.2]) for severe RV-AGE in infants for ROTARIX;
  - 74.0% (95% CI [66.8; 79.9]), i.e. an absolute reduction of 136.9 cases per 1000 person-years for RV-AGE and 98% (95% CI [88.3; 100]) for severe RV-AGE for ROTATEQ.
- The most commonly reported adverse effects after oral vaccination against rotavirus infection are diarrhoea, vomiting, fever and irritability.
- Epidemiological studies carried out after market launch of the rotavirus vaccines have confirmed the efficacy findings and demonstrate, in particular, a relative reduction in the risk of hospitalisation for RV-AGE, depending on vaccine coverage.

- However, the available data collectively confirm an increased risk of AI after oral vaccination against rotavirus infection, primarily in the 7 days immediately after administration of the first dose of vaccine. This increased risk can currently be estimated at approximately 6 cases per 100,000 babies vaccinated. Because of the possible occurrence of this rare but serious side effect, it is essential to instruct families to promptly seek medical advice if faced with a distressed infant who declines to feed in the weeks following vaccination.

- Moreover, the currently available data do not provide answers to questions concerning:
  - the potential risk of selection of replacement circulating strains due to the introduction of mass vaccination;
  - the risk factors for complications of RV-AGE and the possible benefit of identifying a population to be targeted for vaccination;
  - the levels of vaccine cover that will be obtained in the recommended populations in France;
  - the risk of confusion between vaccination against RV-AGE and protection against gastroenteritis.

Benefit of the medicinal product

- The actual benefit* of the rotavirus vaccines ROTARIX and ROTATEQ is insufficient to justify their reimbursement by National Health Insurance.
- Does not recommend 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 17 December 2014 (CT-13564) and is available at **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 for hospital use.