HAUTE AUTORITÉ DE SANTÉ

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TRANSPARENCY COMMITTEE

OPINION

21 October 2009

MENJUGATE KIT powder and solvent for suspension for injection – meningococcal group C oligosaccharide conjugate vaccine (adsorbed)
Pack of 1 vial of powder + 1 syringe prefilled with solvent (CIP: 370 822-5)

Applicant: NOVARTIS VACCINES AND DIAGNOSTICS SA

Neisseria meningitidis group C (strain C11) oligosaccharide conjugated to CRM_{197} protein

ATC Code: J07AH07

List I

Date of initial MA (mutual recognition procedure):
MENJUGATE: 09/07/2002
MENJUGATE KIT: 06/07/2006 – amended: March 11, 2008

Product included on the list of medicines approved for use by hospitals and various public services.

Reason for request: inclusion on the list of products reimbursed by National Insurance for the new population recommended by the High Council for Public Health:
- systematic vaccination for all infants aged 12 to 24 months
- systematic catch-up vaccination up to and including the age of 24 years during the introduction of this new strategy and pending its optimal impact through group immunity.

Additional document:
Opinion of the HCPH regarding vaccination with meningococcal serogroup C conjugate vaccine (sessions of April 24 and June 26, 2006)
http://www.hcsp.fr/docspdf/avisrapports/hcspa20090424_meningC.pdf

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Neisseria meningitidis group C (strain C11) oligosaccharide conjugated to CRM_{197} protein

1.2. Indication

"Active immunisation of infants from the age of 2 months, of children, adolescents and adults to prevent against invasive diseases caused by serogroup C *Neisseria meningitidis*.
MENJUGATE KIT must be used according to official guidelines".

1.3. Dosage (in the newly recommended population)

"Infants over the age of 12 months, children, adolescents and adults: one single dose of 0.5 ml.
Due to limited data, the need for a booster dose has not been established".

2 SIMILAR MEDICINAL PRODUCTS

2.1 ATC Classification (2009)

J	:	Antiinfectives for systemic use
J07	:	Vaccines
J07A	:	Bacterial vaccines
J07AH	:	Meningococcal vaccines
J07AH07	:	Conjugate vaccines

2.2. Medicines in the same therapeutic category

Comparator medicines

There are no comparable vaccines reimbursed by National Insurance under the new vaccine recommendations.

2.3. Medicines with a similar therapeutic aim

Vaccines not recommended by the HCPH among the newly designated population:

Meningococcal A + C polysaccharide vaccine (PASTEUR VACCINS)
Indicated from the age of 18 months (approved for use by hospitals)

MENCEVAX meningococcal A + C+ Y+ W_{135} vaccine (GSK)
Indicated from the age of 24 months (approved for use by hospitals)

3 UPDATE WITH DATA AVAILABLE SINCE PREVIOUS OPINION

3.1. Efficacy

3.1.1. Reminder (Committee's opinion of November 20, 2002)

"Immunogenicity compared to meningococcal non-conjugated polysaccharide vaccines in young children, children, adolescents and adults

Percentage of subjects with titres of meningococcal C bactericidal antibodies ≥ 1: 8 (human complement) 1 month after immunisation with this vaccine or with a meningococcal non-conjugated polysaccharide vaccine (by age group).								
	1-2 years		3-5 years		11-17 years		18-64 years	
	MENJUGATE n=237	MenPS (1) n=153	MENJUGATE n=80	MenPS (1) n=80	MENJUGATE n=90	MenPS (2) n=90	MENJUGATE n=136	MenPS (2) n=130
SBA (Serum Bactericidal Antibodies) %≥ 1 :8 (95%CI) (human complement)	78% (72-83) (S)	19% (13-26)	79% (68 –87) (S)	28% (18-39)	84% (75-91) (S)	68% (57-77)	90% (87-95)	88% (82-93)

MenPS: approved meningococcal non-conjugated polysaccharide vaccine.

(1) = serogroups A, C, W_{135} and Y, containing 50 µg of serogroup C per dose.

(2) = serogroups A and C, containing 50 µg of serogroup C per dose.

S: significant difference

Compared to meningococcal non-conjugated polysaccharide vaccines, the immune response induced by this vaccine is:

- higher in young children, children and adolescents;
- similar in adults.

Contrary to non-conjugated polysaccharide vaccines, this vaccine induces an immune memory after vaccination although the protection duration has not been established.

A booster dose during the second year of life induces an anamnestic response. The need for a booster dose has not yet been established but is currently being evaluated.

Postmarketing surveillance following a vaccination campaign in the UK

"The Public Health services in the UK conducted a postmarketing surveillance programme and analysed the efficacy of three meningococcal serogroup C conjugate vaccines introduced in stages on young children and 15 to 17 year old in the UK:

November 1, 1999	WYETH vaccine	15-17 years
November 29, 1999	WYETH vaccine	Infants
January 10, 2000	WYETH vaccine	Children under the age of 2
March 6, 2000 – May 8, 2000	CHIRON vaccine	9-14 years
April 10, 2000	WYETH vaccine	2-5 years
August 2000	BAXTER vaccine	5-8 years

Sixteen months after the begining of the meningococcal serogroup C conjugate vaccination programme, the preliminary estimates suggested short-term efficacy at:

- 88% for young children (12 to 30 months old)
- 96% for 15 to 17 year olds".

Data updated to March 2004 (SPC of July 6, 2006)

"The efficacy estimates based on a limited number of cases, over one year after the end of priming vaccination, indicate that protection could decrease in young children given a single priming vaccination dose.

In all other age categories (up to 18 years) vaccinated with a single dose, efficacy was maintained at about 90% or more during the year following vaccination and beyond".

3.1.2. Update of data available

No new immunogenicity data has been provided for the population concerned by the new HCPH recommendations.

3.2. Tolerance

3.2.1. Reminder (Committee's opinion of November 20, 2002)

"Very common adverse effects reported are:

- myalgia and arthralgia in adults
- drowsiness among very young children
- headaches among secondary school children and frequently reported in primary school children.

The safety of this vaccine is comparable to that of other conjugate vaccines currently marketed."

3.2.2. Update of data available

The following statement has been added to the SPC adverse effects section:
"very rare visual disorders and photophobia have been reported after vaccination with a group C meningococcal conjugate vaccine, usually associated with other neurological symptoms such as headaches and dizziness".

3.3. Conclusion

This conjugate vaccine is immunogenic in infants, children, adolescents and young adults. However, the duration of longer term protection has not been determined. The need for a late booster dose has not been established in subjects over the age of 12 months.
Data published concerning the impact of prevention strategies in the four countries (UK, Spain, Quebec and the Netherlands) introducing a targeted vaccination strategy with a catch-up campaign demonstrated a substantial decrease in the incidence of invasive meningococcal serogroup C infections from the first year of surveillance (>90%[1]) with a vaccination cover of around 90% in the targeted populations and those concerned by the catch-up programme.

The tolerance of this vaccine is good and comparable to that of other conjugate vaccines currently marketed.

4 CONCLUSIONS OF THE TRANSPARENCY COMMITTEE

4.1. Actual benefit

This vaccine prevents against serious infections that can be fatal.

This product is intended for preventive treatment.

The efficacy (immunogenicity and protective efficacy) / adverse effects ratio is high.

There are no alternative reimbursed vaccines.

Public health benefit

Due to the severity of prognosis and contagiousness, the burden of infectious meningitis can be considered moderate. In France, *Neisseria Meningitidis* is thought to be responsible for 30% of all bacterial meningitis cases and 25 to 30% of *Neisseria Meningitidis* meningitis cases are thought to be attributable to serogroup C. Given the limited number of cases observed in France (175

[1] In the Netherlands: 200 cases/year (2000 to 2002) to 42 cases in 2003 and 17 cases in 2004.

cases reported every year on average through mandatory declaration from 2033 to 2008*), the burden of invasive meningococcal serogroup C infections is therefore only low.

Given recent epidemiological data available in France (increase in the incidence of invasive C meningococcal infections, episodes of grouped cases resulting in the creation of a vaccination programme), the prevention of these infections is now an established health need (High Council for Public Health recommendations in 2009).

The efficacy data for MENJUGATE KIT is based on the immune response and the reported impact of prevention strategies promoted in other European countries. The implementation of vaccination programmes in certain European countries has demonstrated a significant decrease in the incidence of IMI (around 90%).
Subject to a high vaccination coverage, a substantial impact is expected in France in terms of morbidity and mortality in both vaccinated and unvaccinated populations. Indeed, an indirect impact, mainly due to the vaccine's ability to reduce nasopharyngeal carriage in adolescents and young adults, is also expected.

MENJUGATE KIT is therefore likely to provide a solution to an identified public health need.

Consequently, a low public health benefit is expected for MENJUGATE KIT in this indication, as for the other meningococcal C vaccines. This benefit will depend on the vaccination coverage achieved.

* opinion of the High Council for Public Health regarding vaccination with the meningococcal serogroup C conjugate vaccine - sessions of April 24 and June 26, 2009

The actual benefit of this vaccine is substantial.

4.2. Improvement in actual benefit

Taking into account,
- the severity of *Neisseria meningitidis* serogroup C infections,
- the immunogenicity of this vaccine,
- the impact of the prevention strategies conducted in other European countries (infants, children, adolescents, young adults),
- the absence of any available alternative recommended by the High Council for Public Health for infants from the age of 12 months, children, adolescents and adults up to and including the age of 24 years,

this vaccine maintains a major improvement in actual benefit (IAB I) in the prevention of these invasive serogroup C *Neisseria meningitidis* diseases in infants from the age of 12 months, children, adolescents and young adults up to and including the age of 24 years.

The Committee stresses that the efficacy of this prevention strategy is subject to a high vaccination coverage being achieved rapidly and that this strategy and the possible need for a booster during adolescence (not currently established) will be re-assessed according to surveillance data.

4.3. Therapeutic use[2]

According to the High Council for Public Health, vaccination is recommended systematically to infants aged 12 to 24 months with a single meningococcal C conjugate vaccine dose. This systematic vaccination is extended up to and including the age of 24 years using the same single dose vaccination schedule during the introduction of this new strategy and pending its optimal impact through group immunity.

4.4. Target population

The target population of the MENJUGATE KIT vaccine is comprised of:
- all infants aged 12 to 24 months;
- children, adolescents and adults up to and including the age of 24 during the introduction of the strategy.

According to INSEE data, approximately 834,000 infants are aged 12 to 24 months and around 17.6 million children, adolescents and young adults are likely to be included in the catch-up programme. The vaccination coverage for the catch-up programme is difficult to estimate.

4.5. Transparency Committee recommendations

The Transparency Committee recommends inclusion on the list of products reimbursed by National Insurance in the indications and dosages of the MA for the new population recommended by the High Council for Public Health.

4.5.1. Packaging: the packaging is appropriate for prescription requirements

4.5.2. Reimbursement rate: 65%

[2] Opinion of the HCPH regarding vaccination with meningococcal serogroup C conjugate vaccine (sessions of April 24 and June 26, 2006) http://www.hcsp.fr/docspdf/avisrapports/hcspa20090424_meningC.pdf