Nimenrix™

Meningococcal polysaccharide serogroups A, C, W-135 and Y conjugate vaccine

QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains 5 micrograms of polysaccharide for *Neisseria meningitidis* serogroups A[1], C[1], W-135[1] and Y[1].

[1]conjugated to tetanus toxoid carrier protein 44 micrograms

PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

CLINICAL PARTICULARS

Indications

Active immunization of individuals from 12 months of age against invasive meningococcal diseases caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y (see section "*Pharmacodynamics*").

Dosage and Administration

Primary vaccination

A single 0.5 ml dose of the reconstituted vaccine is used for immunization.

Booster vaccination

Nimenrix™ may be given as a booster dose in subjects who have previously been vaccinated with a plain polysaccharide meningococcal vaccine.

There are no data available in subjects previously vaccinated with a meningococcal C conjugate vaccine. The need for a booster dose in subjects primed with ***Nimenrix™*** has not been established.

Nimenrix™ should be used in accordance with available official recommendations.

Nimenrix™ is for intramuscular injection only, preferably in the deltoid muscle.

In children 12 to 23 months of age, the vaccine may also be administered in the anterolateral part of the thigh. (see sections "*Warnings and Precautions*" and "*Interactions*").

Contraindications

Nimenrix™ should not be administered to subjects with hypersensitivity to the active substances or to any of the excipients contained in the vaccine. (see sections "*Qualitative and quantitative composition*" and "*List of excipients*").

Warnings and Precautions

Nimenrix™ should under no circumstances be administered intravascularly, intradermally or subcutaneously.

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

As with other vaccines, vaccination with ***Nimenrix™*** should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

As with other vaccines administered intramuscularly, ***Nimenrix™*** should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

Nimenrix™ will only confer protection against *Neisseria meningitidis* serogroups A, C, W-135 and Y. The vaccine will not protect against other *Neisseria meningitidis* serogroups.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.

Safety and immunogenicity have not been assessed in patients with increased susceptibility to meningococcal infection due to conditions such as terminal complement deficiencies and anatomic or functional asplenia. In these individuals, an adequate immune response may not be elicited.

Although ***Nimenrix™*** contains tetanus toxoid, this vaccine does not substitute for tetanus immunisation.

A more rapid waning of serum bactericidal antibody titres against MenA than for other groups (C, W-135, Y), has been observed when using human complement in the assay (see section "*Pharmacodynamic Effects*"). In individuals expected to be at particular risk of exposure to MenA and who received a first dose of ***Nimenrix™*** more than one year earlier, consideration may be given to administering a second dose of ***Nimenrix™***. Available data indicate that a second dose will elicit an anamnestic immune response to all four meningococcal types in the vaccine. Currently there is very limited information available on the safety of a second dose of ***Nimenrix™***.

Interactions

Nimenrix™ can be given concomitantly with any of the following vaccines: hepatitis A (HAV) and hepatitis B (HBV) vaccines, measles - mumps - rubella (MMR) vaccine, measles - mumps - rubella - varicella (MMRV) vaccine, 10-valent pneumococcal conjugate vaccine or unadjuvanted seasonal influenza vaccine.

Nimenrix™ can also be given concomitantly with combined diphtheria - tetanus - acellular pertussis vaccines in the second year of life, including combination DTaP vaccines with hepatitis B, inactivated polio or Haemophilus influenzae type b, such as DTaP-HBV-IPV/Hib vaccine.

Safety and immunogenicity of ***Nimenrix™*** was evaluated when sequentially administered or co-administered with a DTaP-HBV-IPV/Hib vaccine in the second year of life. The administration of ***Nimenrix™*** one month after the DTaP-HBV-IPV/Hib vaccine resulted in lower MenA, MenC and MenW-135 Geometric Mean Titres (GMTs) as measured with rabbit complement serum bactericidal assay (rSBA). Clinical relevance of this observation is unknown, since at least 99.4% of subjects (N=178) had rSBA titres ≥ 8 for each group (A, C, W-135, Y). Whenever possible, ***Nimenrix™*** and a tetanus toxoid (TT) containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should be co-administered or ***Nimenrix™*** should be administered at least one month before the TT-containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine, lower Geometric Mean antibody Concentrations (GMCs) and opsonophagocytic assay (OPA) antibody GMTs were observed for one pneumococcal serotype (18C conjugated to tetanus toxoid carrier protein). Clinical relevance of this observation is unknown. There was no impact of co-administration on the other nine pneumococcal serotypes.

If ***Nimenrix™*** is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

As with other vaccines it may be expected that in patients receiving immunosuppressive treatment an adequate response may not be elicited.

Pregnancy and Lactation

There is limited experience with use of ***Nimenrix™*** in pregnant women. Animal studies with ***Nimenrix™*** do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryo/foetal development, parturition or post-natal development (see section "*Pre-clinical safety data*").

Nimenrix™ should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

The safety of ***Nimenrix™*** when administered to breast-feeding women has not been evaluated. It is unknown whether ***Nimenrix™*** is excreted in human breast milk.

Nimenrix™ should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Effects on Ability to Drive and Use Machines

No studies on the effects of ***Nimenrix™*** on the ability to drive and use machines have been performed.

Adverse Reactions

The safety profile presented below is based on a pooled analysis on 8,108 subjects who have been vaccinated with one dose of ***Nimenrix™*** in clinical studies.

Adverse reactions reported are listed according to the following frequency:

Very common ≥ 1/10
Common ≥ 1/100 to < 1/10
Uncommon ≥ 1/1000 to < 1/100
Rare ≥ 1/10000 to < 1/1000
Very rare < 1/10000
Not known (cannot be estimated from the available data)

Metabolism and nutrition disorders
Very common: appetite lost

Psychiatric disorders
Very common: irritability
Uncommon: insomnia, crying

Nervous system disorders
Very common: drowsiness, headache
Uncommon: hypoaesthesia, dizziness

Gastrointestinal disorders
Common: gastrointestinal symptoms (including diarrhoea, vomiting and nausea)

Skin and subcutaneous tissue disorders
Uncommon: pruritus, rash

Musculoskeletal and connective tissue disorders
Uncommon: myalgia, pain in extremity

General disorders and administration site conditions
Very common: fever, swelling, pain and redness at injection site, fatigue
Common: injection site haematoma
Uncommon: malaise, injection site reaction (including induration, pruritus, warmth, anaesthesia)

Overdose

No cases of overdose have been reported.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Pharmacotherapeutic group: bacterial vaccines, ATC code J07AH08

Mechanism of Action

Anti-capsular meningococcal antibodies protect against meningococcal diseases via complement mediated bactericidal killing. ***Nimenrix™*** induces the production of bactericidal antibodies against capsular polysaccharides of serogroups A, C, W-135 and Y when measured by assays using either rabbit complement (rSBA) or human complement (hSBA). By conjugating capsular polysaccharide to a protein carrier that contains T-cell epitopes, meningococcal conjugate vaccines like ***Nimenrix™*** change the nature of immune response to capsular polysaccharide from T-cell independent to T-cell dependent.

Pharmacodynamic Effects

The clinical program of ***Nimenrix™*** included 17 clinical studies conducted in 17 countries worldwide. The immunogenicity of one dose of ***Nimenrix™*** has been evaluated in more than 8,000 subjects aged 12 months to 55 years.

Vaccine efficacy was inferred from the demonstration of immunologic non inferiority (based mainly on comparing proportions with rSBA titres at least 1:8) to licensed meningococcal vaccines. Immunogenicity was measured by using rSBA or hSBA which are biomarkers for protective efficacy against meningococcal groups A, C, W-135 and Y.

The vaccine response was defined in subjects aged 2-55 years as the proportion of subjects with:

- rSBA titres ≥ 32 for initially seronegative subjects (i.e, pre-vaccination rSBA titre < 8)
- at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects (i.e., pre-vaccination rSBA titre ≥ 8)

Vaccine immunogenicity

Immunogenicity in toddlers aged 12-23 months

In clinical studies MenACWY-TT-039 and MenACWY-TT-040, the immune response to vaccination with either ***Nimenrix™*** or a licensed meningococcal C-CRM$_{197}$ conjugate (MenC-CRM) vaccine was evaluated.

Table/ Tableau/ Tabla 6

Group Groupe Serogrupo	Response to Réponse à Respuesta a	1 month post-vaccination 1 mois post-vaccination 1 mes posvacunación			1 year persistence Persistance à 1 an Persistencia tras 1 año		
		N	≥8	GMT	N	≥8	GMT
A	***Nimenrix™***	105	80.0 %	53.4	104	16.3%	3.5
	ACWY-PS	35	25.7%	4.1	35	5.7%	2.5
C	***Nimenrix™***	101	89.1%	155.8	105	95.2%	129.5
	ACWY-PS	38	39.5%	13.1	31	32.3%	7.7
W-135	***Nimenrix™***	103	95.1%	133.5	103	100%	256.7
	ACWY-PS	35	34.3%	5.8	31	12.9%	3.4
Y	***Nimenrix™***	89	83.1%	95.1	106	99.1%	265.0
	ACWY-PS	32	43.8%	12.5	36	33.3%	9.3

Table/ Tableau/ Tabla 7

Group Groupe Serogrupo	***Nimenrix™***			ACWY-PS		
	N	≥8	GMT	N	≥8	GMT
A	445	99.8%	1517.4	144	100%	810.6
C	447	99.3%	1121.9	145	98.6%	1499.0
W-135	447	99.6%	2070.6	143	95.1%	442.6
Y	447	100%	3715.9	142	97.2%	1090.3

Table/ Tableau/ Tabla 8

Group Groupe Serogrupo	Response to Réponse à Respuesta a	1 month post-vaccination 1 mois post-vaccination 1 mes posvacunación			1 year persistence Persistance à 1 an Persistencia tras 1 año		
		N	≥8	GMT	N	≥8	GMT
A	***Nimenrix™***	356	82.0%	58.7	350	29.1%	5.4
	ACWY-DT	108	73.1%	41.3	112	31.3%	6.0
C	***Nimenrix™***	359	96.1%	532.0	336	94.9%	172.0
	ACWY-DT	114	99.1%	319.9	105	73.3%	46.7
W-135	***Nimenrix™***	334	91.0%	116.8	327	98.5%	197.5
	ACWY-DT	97	75.3%	71.9	108	75.9%	49.5
Y	***Nimenrix™***	364	95.1%	246.0	356	97.8%	271.8
	ACWY-DT	112	81.3%	103.8	113	86.7%	101.0

Table/ Tableau/ Tabla 9

Group Groupe Serogrupo	Response to Réponse à Respuesta a	Pre-challenge Avant la dose d'épreuve Antes de la provocación		Post-challenge Après la dose d'épreuve Tras la provocación	
		N	GMT	N	GMT
A	***Nimenrix™***	32	544.0	25	3321.9
C	***Nimenrix™***	31	174.0	32	5965.7
	MenC-CRM vaccine	28	34.4	30	5265.2
W-135	***Nimenrix™***	32	643.8	32	11058.1
Y	***Nimenrix™***	32	439.8	32	5736.6

Table/ Tableau/ Tabla 10

Group Groupe Serogrupo	Subjects vaccinated 30 to 42 months previously with ACWY-PS Sujets vaccinés 30 à 42 mois auparavant avec ACWY-PS Sujetos vacunados con ACWY-PS entre los 30 y 42 meses anteriores			Subjects who had not received a meningococcal vaccine in the preceding 10 years Sujets naïfs de vaccin méningococcique au cours des 10 années précédentes Sujetos sin vacunación antimeningocócica en los 10 años anteriores		
	N	≥8	GMT	N	≥8	GMT
A	146	100%	6868.8	69	100%	13014.9
C	169	100%	1945.8	75	100%	5494.6
W-135	169	100%	4635.7	75	100%	9078.0
Y	169	100%	7799.9	75	100%	13895.5

Instructions for Use/Handling
Mode d'emploi / de manipulation
Instrucciones para el empleo/manejo

Instructions for reconstitution of the vaccine with solvent presented in ampoules
Instructions pour la reconstitution du vaccin avec le solvant présenté en ampoules.
Instrucciones para la reconstitución de la vacuna con el solvente presentado en ampollas

Nimenrix™ must be reconstituted by adding the entire content of the ampoule of solvent to the vial containing the powder. To do so, break the top of the ampoule, draw up the solvent with a syringe and add the solvent to the powder. The mixture should be well shaken until the powder is completely dissolved in the solvent.
The reconstituted vaccine is a clear colourless solution.
The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.
After reconstitution, the vaccine should be used immediately.
A new needle should be used to administer the vaccine.

Nimenrix™ doit être reconstitué en ajoutant la totalité du contenu de l'ampoule de solvant dans le flacon de poudre. Pour cela, casser la partie supérieure de l'ampoule, prélever le solvant à l'aide d'une seringue et ajouter le solvant à la poudre. Bien agiter le mélange jusqu'à dissolution complète de la poudre dans le solvant.
Le vaccin reconstitué est une solution limpide et incolore.
Avant l'administration, inspecter le vaccin visuellement pour vérifier l'absence de particules étrangères et (ou) de modification de l'aspect physique. En cas d'anomalie, jeter le vaccin.
Après reconstitution, le vaccin doit être utilisé immédiatement.
Utiliser une aiguille neuve pour administrer le vaccin.

Nimenrix™ debe reconstituirse agregando la totalidad del solvente contenido en la ampolla al vial que contiene el polvo. Para ello, quiebre la parte superior de la ampolla, extraiga el solvente con una jeringa y agréguelo al polvo. La mezcla debe agitarse bien hasta que el polvo se disuelva por completo en el solvente.
La vacuna reconstituida es una solución transparente e incolora.
Antes de la administración, la vacuna reconstituida debe inspeccionarse visualmente para detectar cualquier partícula extraña y/o variación en el aspecto físico. En caso de observar alguna de estas alteraciones, deseche la vacuna.
Después de la reconstitución, la vacuna debe aplicarse inmediatamente.
Debe usarse una nueva aguja para administrar la vacuna.

Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe
Instructions pour la reconstitution du vaccin avec le solvant présenté en seringue pré-remplie.
Instrucciones para la reconstitución de la vacuna con el solvente presentado en jeringa prellenada

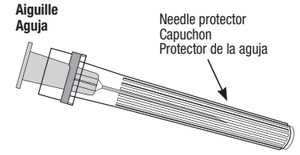
Nimenrix™ must be reconstituted by adding the entire content of the pre-filled syringe of solvent to the vial containing the powder.

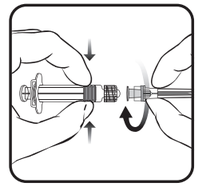
To attach the needle to the syringe, refer to the below drawing. However, the syringe provided with ***Nimenrix™*** might be slightly different than the syringe described in the drawing.

Nimenrix™ doit être reconstitué en ajoutant la totalité du contenu de la seringue préremplie de solvant dans le flacon de poudre.
Se reporter au schéma ci-dessous pour fixer l'aiguille sur la seringue. La seringue fournie avec ***Nimenrix™*** peut toutefois être légèrement différente de celle décrite sur le dessin.

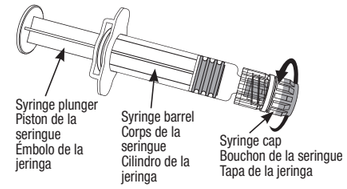
Nimenrix™ debe reconstituirse agregando la totalidad del solvente contenido en la jeringa prellenada al vial que contiene el polvo.
Para colocar la aguja a la jeringa, consulte las ilustraciones que figuran a continuación. Sin embargo, es posible que la jeringa suministrada junto con ***Nimenrix™*** sea levemente diferente de la jeringa descrita en las ilustraciones.

Needle
Aiguille
Aguja





Syringe
Seringue
Jeringa



1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock. (see picture)
3. Remove the needle protector, which on occasion can be a little stiff.

Add the solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.
The reconstituted vaccine is a clear colourless solution.
The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.
After reconstitution, the vaccine should be used immediately.
A new needle should be used to administer the vaccine.
Any unused product or waste material should be disposed of in accordance with local requirements.
Not all presentations are available in every country.

1. En tenant le corps de la seringue dans une main (éviter de tenir le piston), dévisser le bouchon de la seringue en tournant dans le sens inverse des aiguilles d'une montre.
2. Pour fixer l'aiguille sur la seringue tourner l'aiguille dans le sens des aiguilles d'une montre à l'intérieur de la seringue jusqu'à ce qu'elle soit bloquée (voir le dessin)
3. Retirer le capuchon protecteur de l'aiguille, ce qui peut s'avérer parfois un peu dur.

Ajouter le solvant à la poudre. Après avoir ajouté le solvant à la poudre, bien agiter le mélange jusqu'à dissolution complète de la poudre dans le solvant.
Le vaccin reconstitué est une solution limpide et incolore.
Avant l'administration, inspecter le vaccin visuellement pour vérifier l'absence de particules étrangères et (ou) de modification de l'aspect physique. En cas d'anomalie, jeter le vaccin.
Après reconstitution, le vaccin doit être utilisé immédiatement.
Utiliser une aiguille neuve pour administrer le vaccin.
Tout produit non utilisé ou déchet doit être éliminé conformément à la réglementation en vigueur.
Toutes les présentations peuvent ne pas être disponibles dans chaque pays.

1. Sujete el cilindro de la jeringa con una mano (evite sujetar el émbolo de la jeringa) y desenrosque la tapa de la jeringa girándola en sentido contrario a las agujas del reloj.
2. Para colocar la aguja a la jeringa, gire la aguja en sentido de las agujas del reloj hacia el interior de la jeringa hasta que sienta que ha quedado fija (ver imagen).
3. Retire el protector de la aguja, que en ocasiones puede estar un poco apretado.

Agregue el solvente al polvo. Después de agregar el solvente al polvo, la mezcla debe agitarse bien hasta que el polvo se disuelva por completo en el solvente.
La vacuna reconstituida es una solución transparente e incolora.
Antes de la administración, la vacuna reconstituida debe inspeccionarse visualmente para detectar cualquier partícula extraña y/o variación en el aspecto físico. En caso de observar alguna de estas alteraciones, deseche la vacuna.
Después de la reconstitución, la vacuna debe aplicarse inmediatamente.
Debe usarse una nueva aguja para administrar la vacuna.
Todo producto no utilizado o material desechable debe eliminarse de acuerdo con los requisitos locales.
No todas las presentaciones existen en todos los países.

Nimenrix is a trademark of the GlaxoSmithKline group of companies
Nimenrix est un nom de marque des sociétés du groupe GlaxoSmithKline.
Nimenrix es una marca registrada del grupo de compañías GlaxoSmithKline.

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Nimenrix™

GlaxoSmithKline

Nimenrix™ elicited a bactericidal antibody response against the four groups, with a response against group C that was comparable to the one elicited by the licensed MenC-CRM vaccine in term of rSBA titres ≥8 (Table 1).

Table 1: Bactericidal antibody responses (rSBA) in toddlers aged 12-23 months

In the study MenACWY-TT-039, the serum bactericidal activity was also measured using human serum as the source of complement (hSBA) as a secondary endpoint (Table 2).

Table 2: Bactericidal antibody responses (hSBA) in toddlers aged 12-23 months

Immunogenicity in children aged 2-10 years

In two comparative studies conducted in subjects aged 2-10 years, one group of subjects received a dose of ***Nimenrix™*** and a second group a dose of either a licensed MenC-CRM vaccine (study MenACWY-TT-081) or the licensed GlaxoSmithKline Biologicals' plain polysaccharide meningococcal group A, C, W-135, Y (ACWY-PS) vaccine (study MenACWY-TT-038) as comparator.

In the MenACWY-TT-038 study, ***Nimenrix™*** was demonstrated to be non-inferior to the licensed ACWY-PS vaccine in terms of vaccine response to the four groups (A, C, W-135 and Y) (Table 3).

Table 3: Bactericidal antibody responses (rSBA) to *Nimenrix™* and the ACWY-PS vaccine in children aged 2-10 years 1 month after vaccination (study MenACWY-TT-038)

In the MenACWY-TT-081 study, ***Nimenrix™*** (N=268) was demonstrated to be non-inferior to another licensed MenC-CRM vaccine (N=92) in terms of vaccine response to the Men C group (94.8% and 95.7% respectively), GMTs were lower for the ***Nimenrix™*** group (2794.8) versus the MenC-CRM vaccine (5291.6).

Immunogenicity in adolescents aged 11-17 years and adults aged ≥ 18 years

In two clinical studies, conducted in adolescents 11-17 years of age (study MenACWY-TT-036) and in adults 18-55 years of age (study MenACWY-TT-035), either one dose of ***Nimenrix™*** or one dose of the ACWY-PS vaccine were administered.

In both adolescents and adults, ***Nimenrix™*** was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine in terms of vaccine response. The response to the four meningococcal groups elicited by ***Nimenrix™*** was either similar or higher than the one elicited by the ACWY-PS vaccine (Table 4).

Table 4: Bactericidal antibody responses (rSBA) to *Nimenrix™* and the ACWY-PS vaccine in adolescents aged 11-17 years and adults aged ≥ 18 years 1 month after vaccination

Persistence of immune response

The persistence of the immune response elicited by ***Nimenrix™*** was evaluated 12 to 42 months after vaccination in subjects aged 12 months to 55 years.

In all age groups, the rSBA GMTs observed at the persistence time-point were higher than prior to vaccination for the four groups.

For all groups (A, C, W-135, Y), the persistence of the antibodies elicited by ***Nimenrix™*** was similar or higher than those induced by the licensed meningococcal vaccines (i.e. MenC-CRM vaccine in subjects aged 12-23 months and ACWY-PS vaccine in subjects older than 2 years of age).

In contrast to the observed rSBA-MenA persistence, across age groups, there was a more rapid waning (as measured at 12 months post-dose onwards) of serum bactericidal antibody titres against MenA than against other groups (C, W-135, Y) when using human complement in the assay (Tables 5, 6 and 8). This rapid waning of hSBA-MenA antibodies has also been observed with other meningococcal vaccines. The clinical relevance of the rapid waning of hSBA-MenA antibody titres is unknown (see section "*Warnings and Precautions*").

Persistence of immune response in toddlers aged 12-23 months

In study MenACWY-TT-048, the persistence of the immune response was evaluated by rSBA and hSBA 2 years after vaccination in toddlers primed in study MenACWY-TT-039 (Table 5).

Table 5: 2 year persistence data in toddlers aged 12-23 months at vaccination

Persistence of immune response in children aged 6-10 years

In study MenACWY-TT-028, the persistence of the immune response was evaluated by hSBA 1 year after vaccination in children 6-10 years of age primed in study MenACWY-TT-027 (Table 6).

Table 6: 1 month post-vaccination and 1 year persistence data in children 6-10 years of age

Persistence of immune response in adolescents aged 11-17 years

In study MenACWY-TT-043, the persistence of the immune response was evaluated 2 years after vaccination in adolescents primed in study MenACWY-TT-036 (Table 7). See Table 4 for primary results in this study.

Table 7: 2 year persistence data (rSBA) in adolescents aged 11-17 years at vaccination

Persistence of immune response in adolescents and adults aged 11-25 years evaluated by hSBA

In study MenACWY-TT-059, the persistence of the immune response was evaluated by hSBA 1 year after vaccination in adolescents and adults 11-25 years of age primed in study MenACWY-TT-052.
For all groups (A, C, W-135, Y), the persistence of the antibodies elicited by ***Nimenrix™*** was similar or higher than those induced by the licensed quadrivalent meningococcal diphtheria toxoid (DT) conjugate vaccine (ACWY-DT) (Table 8).

Table 8: 1 month post-vaccination and 1 year persistence data in adolescents and adults 11-25 years of age evaluated by hSBA

Immune memory

In the study MenACWY-TT-014, the induction of immune memory was assessed one month after the administration of a fifth of the dose of ACWY-PS vaccine (10 µg of each polysaccharide) to children in the third year of life previously primed in the study MenACWY-TT-013 with ***Nimenrix™*** or a licensed MenC-CRM vaccine at the age of 12 to 14 months.

One month after the challenge dose, the GMTs elicited by the subjects primed with ***Nimenrix™*** increased by 6.5 to 8 fold for groups A, C, W-135 and Y and indicate that ***Nimenrix™*** induces immune memory to groups A, W-135 and Y. The post-challenge rSBA-MenC GMT was similar in both study groups, indicating that ***Nimenrix™*** induces an analogous immune memory to group C as the licensed MenC-CRM vaccine (Table 9).

Table 9: Immune response (rSBA) 1 month after a challenge vaccination in subjects primed with *Nimenrix™* or a MenC-CRM vaccine at the age of 12 to 14 months

Immunogenicity in subjects previously vaccinated with a plain polysaccharide meningococcal vaccine

In study MenACWY-TT-021 conducted in subjects aged 4.5-34 years, the immunogenicity of ***Nimenrix™*** administered between 30 and 42 months after vaccination with the ACWY-PS vaccine was compared to the immunogenicity of ***Nimenrix™*** administered to age-matched subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to ***Nimenrix™*** (Table 10). Clinical relevance of this observation is unknown since all subjects achieved rSBA titres ≥ 8 for each group (A, C, W-135, Y).

Table 10: Immune response (rSBA) 1 month after *Nimenrix™* vaccination in subjects according to their meningococcal vaccine history

Pharmacokinetics

Not relevant for vaccines.

Clinical Studies

See section "*Pharmacodynamics*".

Pre-clinical Safety Data

Non-clinical data reveal no special hazard for humans based on local tolerance, acute toxicity, repeated dose toxicity, developmental/reproductive toxicity and fertility studies.

PHARMACEUTICAL PARTICULARS

List of Excipients

Powder: sucrose, trometamol.
Solvent: sodium chloride, water for injections.

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf Life

The expiry date is indicated on the label and packaging.

Special Precautions for Storage

- Store in a refrigerator (2°C – 8°C)
- The solvent may also be stored at ambient temperature (25°C)
- Do not freeze
- Protect from light

Nature and Contents of Container

- Powder in a vial containing 1 dose (type I glass) with a stopper (butyl rubber) and 0.5 ml of solvent for 1 dose in a pre-filled syringe with a stopper (butyl rubber).
  Pack sizes of 1 and 10 with or without needles.
- Powder in a vial containing 1 dose (type I glass) with a stopper (butyl rubber) and 0.5 ml of solvent for 1 dose in an ampoule (type I glass).
  Pack sizes of 1, 10 and 100
  The powder is white. The solvent is clear and colorless.

Instructions for Use/Handling (see at the end of the leaflet)