

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

NIMENRIX^â PRODUCT INFORMATION

NAME OF THE MEDICINE

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

DESCRIPTION

NIMENRIX is supplied as a white powder in a glass vial, together with a clear and colourless solvent supplied in a pre-filled syringe or ampoule.

After reconstitution, 1 dose (0.5 ml) contains:

Meningococcal polysaccharide - Serogroup A ¹	5 micrograms
Meningococcal polysaccharide - Serogroup C ¹	5 micrograms
Meningococcal polysaccharide - Serogroup W-135 ¹	5 micrograms
Meningococcal polysaccharide - Serogroup Y ¹	5 micrograms
¹ conjugated to tetanus toxoid carrier protein	44 micrograms

Other ingredients

The powder for reconstitution also contains the excipients, trometamol and sucrose. The diluent contains 0.9% sodium chloride in water for injections.

No preservative or adjuvant is added.

CLINICAL PHARMACOLOGY

Mechanism of Action

Anti-capsular meningococcal antibodies protect against meningococcal diseases via complement mediated bactericidal activity. NIMENRIX induces the production of bactericidal antibodies against capsular polysaccharides of serogroups A, C, W-135 and Y when measured by serum bactericidal antibody assays (SBA) 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 the immune response to capsular polysaccharide from T-cell independent to T-cell dependent.

CLINICAL TRIALS

Immunogenicity

The clinical development 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 compared to licensed meningococcal vaccines. Immunogenicity was measured by rSBA or hSBA which are biomarkers for protective efficacy against meningococcal groups A, C, W-135 and Y.

Vaccine response was defined in clinical studies as:

rSBA

- Toddlers aged 12-23 months: rSBA \geq 1:8
- Children aged > 2 years, adolescents and adults: rSBA \geq 1:32 for initially seronegative subjects; or at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects

hSBA

- At least a 2-fold increase in hSBA titre (i.e hSBA \geq 1:8) from pre- to post-vaccination for initially seronegative subjects of all ages
- At least a 4-fold increase in hSBA titre from pre- to post-vaccination for initially seropositive subjects of all ages

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-CRM₁₉₇ conjugate (MenC-CRM) vaccine was evaluated.

NIMENRIX elicited a protective bactericidal antibody response against the four serogroups in both studies, with a response against serogroup C that was comparable to the one elicited by the licensed MenC-CRM vaccine in terms of rSBA titres \geq 8 (Table 1).

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

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

Sero-group	Vaccine	Study MenACWY-TT-039 rSBA ⁽¹⁾			Study MenACWY-TT-040 rSBA ⁽²⁾		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	354	99.7% (98.4; 100)	2205.0 (2007.8; 2421.6)	183	98.4% (95.3; 99.7)	3169.9 (2577.2; 3898.8)
C	NIMENRIX	354	99.7% (98.4; 100)	477.6 (437.3; 521.6)	183	97.3% (93.7; 99.1)	828.7 (672.4; 1021.4)
	MenC-CRM	121	97.5% (92.9; 99.5)	212.3 (170.0; 265.2)	114	98.2% (93.8; 99.8)	691.4 (520.8; 917.9)
W-135	NIMENRIX	354	100% (99.0; 100)	2681.7 (2453.1; 2931.6)	186	98.4% (95.4; 99.7)	4022.3 (3269.2; 4948.8)
Y	NIMENRIX	354	100% (99.0; 100)	2729.4 (2472.7; 3012.8)	185	97.3% (93.8; 99.1)	3167.7 (2521.9; 3978.9)

The analysis of immunogenicity was conducted on the according-to-protocol (ATP) cohorts for immunogenicity.

⁽¹⁾ blood sampling performed 42 to 56 days post vaccination

⁽²⁾ blood sampling performed 30 to 42 days post vaccination

N = number of subjects with available results

GMT = geometric mean antibody titre

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

Serogroup	Vaccine	N	Study MenACWY-TT-039 hSBA ⁽¹⁾	
			≥8 (95% CI)	GMT (95%CI)
A	NIMENRIX	338	77.2% (72.4; 81.6)	19.0 (16.4; 22.1)
C	NIMENRIX	341	98.5% (96.6; 99.5)	196.0 (175.4; 219.0)
	MenC-CRM	116	81.9% (73.7; 88.4)	40.3 (29.5; 55.1)
W-135	NIMENRIX	336	87.5% (83.5 ; 90.8)	48.9 (41.2; 58.0)
Y	NIMENRIX	329	79.3%	30.9

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

			(74.5; 83.6)	(25.8; 37.1)
--	--	--	--------------	--------------

The analysis of immunogenicity was conducted on ATP cohort for immunogenicity.

⁽¹⁾ blood sampling performed 42 to 56 days post vaccination

N = number of subjects with available results

GMT = geometric mean antibody titre

Immunogenicity in children aged 2-10 years

In two comparative studies of non-inferiority conducted in subjects aged 2-10 years, one dose of NIMENRIX was compared to either the licensed GlaxoSmithKline Biologicals' plain polysaccharide meningococcal serogroup A, C, W-135, Y (ACWY-PS) vaccine (study MenACWY-TT-038) or a licensed MenC-CRM vaccine (study MenACWY-TT-081).

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 serogroups (A, C, W-135 and Y) (Table 3).

Table 3: Bactericidal antibody responses (rSBA) to NIMENRIX compared with ACWY-PS vaccine in children aged 2-10 years one month after vaccination (study MenACWY-TT-038)

Serogroup	NIMENRIX			ACWY-PS vaccine		
	N	VR (95%CI)	GMT (95%CI)	N	VR (95%CI)	GMT (95%CI)
A	638	88.6% (85.8; 90.9)	6309.7 (5979.0; 6658.8)	206	65.5% (58.6; 72.0)	2309.4 (2055.8; 2594.3)
C	732	95.9% (94.2; 97.2)	4983.6 (4514.1; 5502.0)	251	89.6% (85.2; 93.1)	1386.8 (1108.9; 1734.4)
W-135	738	97.4% (96.0; 98.4)	11569.8 (10910.7; 12268.7)	252	82.5% (77.3; 87.0)	2150.6 (1823.9; 2535.8)
Y	771	92.5% (90.4; 94.2)	10886.6 (10310.7; 11494.5)	258	68.6% (62.6; 74.2)	2544.7 (2178.2; 2972.9)

The analysis of immunogenicity was conducted on ATP cohort for immunogenicity.

VR: vaccine response, defined as rSBA titres ≥ 32 for initially seronegative subjects or at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects

N = number of subjects with available results

GMT = geometric mean antibody titre

In the MenACWY-TT-081 study, NIMENRIX (N=268) was demonstrated to be non-inferior to a licensed MenC-CRM vaccine (N=92) in 2 to 10 year olds in terms of serogroup C vaccine response one month post-vaccination [94.8% (95% CI: 91.4; 97.1) and 95.7%

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

(95% CI: 89.2; 98.8) respectively]. Serogroup C geometric mean titres (GMTs) were lower for the NIMENRIX group [2794.8 (95% CI: 2393.5; 3263.3)] versus the MenC-CRM group [5291.6 (95% CI: 3814.6; 7340.5)].

Immunogenicity in adolescents aged 11-17 years and adults aged 18-55 years

In two clinical studies, one dose of NIMENRIX was compared to one dose of ACWY-PS vaccine administered to adolescents aged 11-17 years (study MenACWY-TT-036) and in adults aged 18-55 years (study MenACWY-TT-035).

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

Table 4: Bactericidal antibody responses (rSBA) to NIMENRIX compared with ACWY-PS vaccine in adolescents aged 11-17 years and adults aged 18-55 years one month after vaccination

Study (Age range)	Sero-group	NIMENRIX			ACWY-PS vaccine		
		N	VR (95%CI)	GMT (95%CI)	N	VR (95%CI)	GMT (95%CI)
MenACWY-TT-036 (11-17 years)	A	615	85.4% (82.3; 88.1)	6106.8 (5739.5; 6497.6)	215	79.5% (73.5; 84.7)	3203.0 (2854.1; 3594.6)
	C	719	97.1% (95.6; 98.2)	12645.5 (11531.8; 13866.7)	237	96.6% (93.5; 98.5)	8271.6 (6937.3; 9862.4)
	W-135	717	96.5% (94.9; 97.7)	8390.1 (7777.8; 9050.7)	242	88.0% (83.2; 91.8)	2679.3 (2363.7; 3037.2)
	Y	737	93.1% (91.0; 94.8)	13865.2 (12968.1; 14824.4)	246	78.0% (72.3; 83.1)	5245.3 (4644.2; 5924.1)
MenACWY-TT-035 (18-55 years)	A	743	80.1% (77.0; 82.9)	3624.7 (3371.7; 3896.8)	252	69.8% (63.8; 75.4)	2127.2 (1909.2; 2370.1)
	C	849	91.5% (89.4; 93.3)	8865.9 (8011.0; 9812.0)	288	92.0% (88.3; 94.9)	7371.2 (6297.4; 8628.2)
	W-135	860	90.2% (88.1; 92.1)	5136.2 (4698.8; 5614.3)	283	85.5% (80.9; 89.4)	2461.3 (2081.0; 2911.0)
	Y	862	87.0% (84.6; 89.2)	7710.7 (7100.1; 8320.3)	288	78.8% (73.6; 83.4)	4314.3 (3782.1; 4846.5)

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

				8373.8)			4921.5)
--	--	--	--	---------	--	--	---------

The analysis of immunogenicity was conducted on ATP cohorts for immunogenicity.

VR: vaccine response, defined as rSBA titres ≥ 32 for initially seronegative subjects or at least a 4-fold increase in rSBA titres from pre- to post-vaccination for initially seropositive subjects

N = number of subjects with available results

GMT = geometric mean antibody titre

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 at the time of vaccination.

In all age groups at all persistence time-points measured, the rSBA GMTs remained higher than prior to vaccination for the four serogroups (A, C, W-135, Y).

For all serogroups (A, C, W-135, Y), the persistence of the antibodies elicited by NIMENRIX was similar or higher than those induced by the licensed comparator 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).

Across age groups, there was a rapid waning (as measured at 12 months post-dose onwards) of serum bactericidal antibody titres against MenA when evaluated by hSBA as compared to rSBA (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 "Precautions").

Persistence of immune response in toddlers aged 12-23 months at vaccination

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

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

Sero-group	Vaccine	rSBA			hSBA		
		N	≥ 8 (95%CI)	GMT (95%CI)	N	≥ 8 (95%CI)	GMT (95%CI)
A	NIMENRIX	181	97.8% (94.4; 99.4)	420.3 (356.1; 495.9)	183	23.0% (17.1; 29.7)	3.8 (3.2; 4.5)
C	NIMENRIX	186	88.2%	98.1	175	86.9%	50.2

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

			(82.6; 92.4)	(77.7; 123.8)		(80.9; 91.5)	(38.7; 65.1)
	MenC-CRM	29	69.0% (49.2; 84.7)	53.5 (25.5; 112.0)	19	52.6% (28.9; 75.6)	10.4 (4.4; 22.8)
W-135	NIMENRIX	188	98.9% (96.2; 99.9)	369.9 (342.0; 460.5)	180	91.1% (86.0; 94.8)	77.7 (61.8; 97.6)
Y	NIMENRIX	188	97.9% (94.6; 99.4)	396.6 (324.0; 485.5)	154	87.0% (80.7; 91.9)	58.1 (44.5; 75.8)

The analysis of immunogenicity was conducted on ATP cohort for persistence.

N = number of subjects with available results

GMT = geometric mean antibody titre

Persistence of immune response in children aged 6-10 years at vaccination

In study MenACWY-TT-028, the persistence of the immune response was evaluated by hSBA one year after vaccination in children primed at 6-10 years of age with either NIMENRIX or ACWY-PS vaccine in study MenACWY-TT-027 (Table 6).

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

Sero-group	Vaccine	1 month post-vaccination hSBA			1 year persistence hSBA		
		N	³ 8 (95%CI)	GMT (95%CI)	N	³ 8 (95%CI)	GMT (95%CI)
A	NIMENRIX	105	80.0 % (71.1; 87.2)	53.4 (37.3; 76.2)	104	16.3% (9.8; 24.9)	3.5 (2.7; 4.4)
	ACWY-PS	35	25.7% (12.5;43.3)	4.1 (2.6;6.5)	35	5.7% (0.7;19.2)	2.5 (1.9;3.3)
C	NIMENRIX	101	89.1% (81.3;94.4)	155.8 (99.3;244.3)	105	95.2% (89.2;98.4)	129.5 (95.4;175.9)
	ACWY-PS	38	39.5% (24.0;56.6)	13.1 (5.4;32.0)	31	32.3% (16.7;51.4)	7.7 (3.5;17.3)
W-135	NIMENRIX	103	95.1% (89.0;98.4)	133.5 (99.9;178.4)	103	100% (96.5;100)	256.7 (218.2;301.9)
	ACWY-PS	35	34.3% (19.1;52.2)	5.8 (3.3;9.9)	31	12.9% (3.6;29.8)	3.4 (2.0;5.8)
Y	NIMENRIX	89	83.1% (73.7;90.2)	95.1 (62.4;145.1)	106	99.1% (94.9;100)	265.0 (213.0;329.6)
	ACWY-PS	32	43.8% (26.4;62.3)	12.5 (5.6;27.7)	36	33.3% (18.6;51.0)	9.3 (4.3;19.9)

The analysis of immunogenicity was conducted on ATP cohort for persistence.

N = number of subjects with available results

GMT = geometric mean antibody titre

Persistence of immune response in adolescents aged 11-17 years at vaccination

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

In study MenACWY-TT-043, the persistence of the immune response was evaluated two years after vaccination in adolescents primed with either NIMENRIX or ACWY-PS vaccine in study MenACWY-TT-036 (Table 7). See Table 4 for the primary vaccination results from study MenACWY-TT-036.

Table 7: Two year persistence data in adolescents aged 11-17 years at vaccination

Serogroup	NIMENRIX rSBA			ACWY-PS vaccine rSBA		
	N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	445	99.8% (98.8; 100)	1517.4 (1399.7; 1645.1)	144	100% (97.5; 100)	810.6 (695.9; 944.3)
C	447	99.3% (98.1; 99.9)	1121.9 (996.9; 1262.6)	145	98.6% (95.1; 99.8)	1499.0 (1119.6; 2006.8)
W-135	447	99.6% (98.4; 99.9)	2070.6 (1869.6; 2293.0)	143	95.1% (90.2; 98.0)	442.6 (341.8; 573.0)
Y	447	100% (99.2; 100)	3715.9 (3409.3; 4049.9)	142	97.2% (92.9; 99.2)	1090.3 (857.7; 1386.1)

The analysis of immunogenicity was conducted on ATP cohort for persistence.

N = number of subjects with available results

GMT = geometric mean antibody titre

Persistence of immune response in adolescents and adults aged 11-25 years at vaccination

In study MenACWY-TT-059, the persistence of the immune response was evaluated by hSBA one year after vaccination in adolescents and adults 11-25 years of age primed in study MenACWY-TT-052. For all serogroups (A, C, W-135, Y), the persistence of 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: One month post-vaccination and one year persistence data in adolescents and adults 11-25 years of age at vaccination

Sero-group	Vaccine	1 month post-vaccination hSBA			1 year persistence hSBA		
		N	≥8 (95%CI)	GMT (95%CI)	N	≥8 (95%CI)	GMT (95%CI)
A	NIMENRIX	356	82.0% (77.6; 85.9)	58.7 (48.6; 70.9)	350	29.1% (24.4; 34.2)	5.4 (4.5; 6.4)

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

	ACWY-DT	108	73.1% (63.8; 81.2)	41.3 (27.7; 61.5)	112	31.3% (22.8; 40.7)	6.0 (4.3; 8.4)
C	NIMENRIX	359	96.1% (93.5; 97.9)	532.0 (423.8; 667.8)	336	94.9% (92.0; 97.0)	172.0 (142.5; 207.4)
	ACWY-DT	114	99.1% (95.2; 100)	319.9 (220.0; 465.2)	105	73.3% (63.8; 81.5)	46.7 (30.2; 72.1)
W-135	NIMENRIX	334	91.0% (87.4; 93.9)	116.8 (96.8; 141.0)	327	98.5% (96.5; 99.5)	197.5 (173.0; 225.5)
	ACWY-DT	97	75.3% (65.5; 83.5)	71.9 (44.8; 115.4)	108	75.9% (66.7; 83.6)	49.5 (33.0; 74.4)
Y	NIMENRIX	364	95.1% (92.3; 97.0)	246.0 (207.7; 291.4)	356	97.8% (95.6; 99.0)	271.8 (237.5; 311.2)
	ACWY-DT	112	81.3% (72.8; 88.0)	103.8 (68.0; 158.5)	113	86.7% (79.1; 92.4)	101.0 (69.9; 145.9)

The analysis of immunogenicity was conducted on ATP cohort for persistence

N = number of subjects with available results

GMT = geometric mean antibody titre

Immune memory

In study MenACWY-TT-014, the induction of immune memory was assessed one month after the administration of a one fifth dose of ACWY-PS vaccine (10 µg of each polysaccharide) to children in the third year of life. These children were previously primed in study MenACWY-TT-013 with either 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 6.5 to 8-fold, indicating that NIMENRIX induces immune memory to all four serogroups A, C, 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 serogroup C as the licensed MenC-CRM vaccine (Table 9).

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

Serogroup	Vaccine	Pre-challenge		Post-challenge	
		N	rSBA GMT (95%CI)	N	rSBA GMT (95%CI)
A	NIMENRIX	32	544.0 (325.0; 910.7)	25	3321.9 (2294.2; 4810.0)
C	NIMENRIX	31	174.0 (104.8; 288.9)	32	5965.7 (4128.4; 8620.7)
	MenC-CRM	28	34.4 (15.8; 75.3)	30	5265.2 (3437.3; 8065.1)
W-135	NIMENRIX	32	643.8 (394.1; 1051.8)	32	11058.1 (8587.2; 14239.9)
Y	NIMENRIX	32	439.8	32	5736.6

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

			(274.0; 705.9)		(4215.9; 7806.0)
--	--	--	----------------	--	------------------

The analysis of immunogenicity was conducted on ATP cohort for immunogenicity.

N = number of subjects with available results

GMT = geometric mean antibody titre

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 an 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 serogroup (A, C, W-135, Y) regardless of meningococcal vaccination history.

Table 10: Immune response (rSBA) one month after NIMENRIX vaccination in subjects according to their meningococcal vaccine history

Sero-group	Subjects vaccinated 30 to 42 months previously with ACWY-PS			Subjects who had not received a meningococcal vaccine in the preceding 10 years		
	N	rSBA ≥ 8 (95%CI)	GMT (95%CI)	N	rSBA ≥ 8 (95%CI)	GMT (95%CI)
A	146	100% (97.5; 100)	6868.8 (6044.9; 7805.0)	69	100% (94.8; 100)	13014.9 (10722.2; 15798.0)
C	169	100% (97.8; 100)	1945.8 (1583.3; 2391.1)	75	100% (95.2; 100)	5494.6 (4266.3; 7076.5)
W-135	169	100% (97.8; 100)	4635.7 (3942.5; 5450.7)	75	100% (95.2; 100)	9078.0 (7087.7; 11627.1)
Y	169	100% (97.8; 100)	7799.9 (6682.8; 9103.6)	75	100% (95.2; 100)	13895.5 (11186.2; 17260.9)

The analysis of immunogenicity was conducted on ATP cohort for immunogenicity.

N = number of subjects with available results

GMT = geometric mean antibody titre

Non-clinical information

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

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

INDICATIONS

NIMENRIX is indicated for active immunisation of individuals from the age of 12 months through 55 years against invasive meningococcal diseases caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y.

CONTRAINDICATIONS

NIMENRIX should not be administered to subjects with hypersensitivity to the active substances or to any of the excipients contained in the vaccine.

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.

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

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 serogroups (C, W-135, Y), has been observed when using human complement in the assay (see "Clinical Trials, Persistence of immune response"). In individuals expected to be at particular risk of exposure to MenA and who received a first dose of NIMENRIX more than one year prior, 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.

Subjects previously vaccinated with a plain polysaccharide meningococcal vaccine and vaccinated with Nimenrix 30 to 42 months later had lower Geometric Mean Titres (GMTs) measured with rabbit complement serum bactericidal assay (rSBA) than subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years (see Table 10 in Clinical Trial section and Study 021). Clinical relevance of this observation is unknown.

Paediatric population

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

The safety and efficacy of Nimenrix in children under 12 months of age has not been established.

Elderly population

There are no data in individuals older than 55 years of age.

Effects on Fertility

Animal studies with NIMENRIX do not indicate direct or indirect harmful effects with respect to fertility (see “Non-clinical information”).

Use in Pregnancy (Category B2):

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 pregnancy, embryo/foetal development, parturition or post-natal development (see “Non-clinical information”).

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

Use in Lactation:

The safety of NIMENRIX when administered to breastfeeding 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.

Carcinogenicity:

The carcinogenic potential of NIMENRIX has not been investigated

Ability to perform tasks that require judgement, motor or cognitive skills:

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

INTERACTIONS WITH OTHER MEDICINES

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

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 (DTaP) vaccines in the second year of life, including combination DTaP vaccines with hepatitis B, inactivated polio (IPV) or *Haemophilus influenzae* type b (Hib), 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 GMTs as measured with rSBA. Clinical relevance of this observation is unknown, since at least 99.4% of subjects (N=178) had rSBA titres ≥ 8 for each serogroup (A, C, W-135, Y). Whenever possible, NIMENRIX and a tetanus toxoid (TT) containing vaccine, such as DTaP-HBV-IPV/Hib vaccine, should either 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.

ADVERSE EFFECTS

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:

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

Very common	≥ 1/10
Common	≥ 1/100 to < 1/10
Uncommon	≥ 1/1,000 to < 1/100
Rare	≥ 1/10,000 to < 1/1,000
Very rare	< 1/10,000

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)

DOSAGE AND ADMINISTRATION

Primary vaccination

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

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

Booster vaccination

NIMENRIX may be given in subjects who have previously been vaccinated with a plain polysaccharide meningococcal 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.

Method of administration

NIMENRIX is for single use in one patient only.

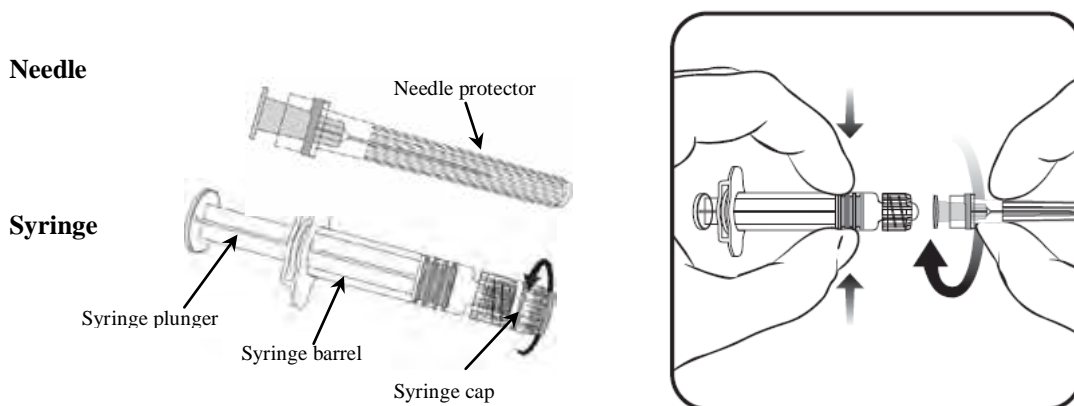
NIMENRIX is for intramuscular injection only, preferably in the deltoid muscle.

In children 12 to 23 months of age, the vaccine may also be administered in the anterolateral part of the thigh. (see "PRECAUTIONS" and "INTERACTIONS").

Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe

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

To attach the needle to the syringe, refer to the below picture.



Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach a screw-thread needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture). A needle without a screw-thread may also be used. In this case, the needle should be attached without screwing.
3. Remove the needle protector, which on occasion can be a little stiff.
4. 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.

Instructions for reconstitution of the vaccine with solvent presented in ampoules

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.

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

Incompatibilities

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

OVERDOSAGE

No cases of overdose have been reported.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

PRESENTATION AND STORAGE CONDITIONS

Presentation

NIMENRIX is supplied as a white lyophilised powder in a glass vial (type 1 glass) with a stopper (butyl rubber), together with 0.5ml solvent either in a glass ampoule (type I glass) or a pre-filled syringe with a stopper (butyl rubber).

Pack sizes of 1 and 10 without separate needles.

Not all pack sizes or presentations may be distributed in Australia.

Storage Conditions

NIMENRIX must be stored between +2°C to +8°C. The sterile 0.9% saline diluent may be refrigerated or stored at ambient temperatures, but must not be frozen. The vaccine should be stored in the original package in order to protect from light.

The shelf-life of NIMENRIX is three years from the date of manufacture when stored at temperatures between +2°C to +8°C. The expiry date of the vaccine is marked on the label and packaging. After reconstitution, the vaccine should be used immediately.

NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Australia Pty Ltd
Level 4, 436 Johnston Street
Abbotsford, Victoria, 3067

Attachment 1: Product information for AusPAR Nimenrix Meningococcal (groups A, C, W-135, Y) polysaccharide tetanus toxoid conjugate vaccine GlaxoSmithKline Australia Pty Ltd PM-2012-01958-3-2 Date of Finalisation 4 December 2013. This Product Information was approved at the time this AusPAR was published.

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG):
29 August 2013

NIMENRIX[®] is a registered trade mark of the GlaxoSmithKline group of companies.

Version 1.0