Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

MENJUGATE KIT 10 micrograms powder and solvent for suspension for injection

Meningococcal group C conjugate vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml of the reconstituted vaccine) contains:

Neisseria meningitidis group C (strain C11) oligosaccharide	10 micrograms
Conjugated to	
Corynebacterium diphtheriae CRM197 protein [1]	12.5 to 25.0 micrograms
adsorbed on aluminium hydroxide	0.3 to 0.4 mg Al^{3+}

[1]CRM197 (Cross Reacting Material 197)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

Powder (vial): white to off-white

Suspension (syringe): white opalescent

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Active immunisation of children from 2 months of age, adolescents and adults, for the prevention of invasive disease caused by *Neisseria meningitidis* group C.
The use of Menjugate Kit should be determined on the basis of official recommendations.

4.2 Posology and method of administration

Posology

Paediatric population

Primary immunisation
Infants from 2 months of age up to 12 months: two doses, each of 0.5 ml, should be given with an interval of at least 2 months between the doses (see section 4.5 regarding co-administration of Menjugate Kit with other vaccines).

Children over the age of 12 months: a single dose of 0.5 ml.

The safety and efficacy of Menjugate Kit in children aged less than 2 months have not been established. No data are available.

Booster doses
It is recommended that a booster dose should be given after completion of the primary immunisation series in infants. The timing of this dose should be in accordance with available official recommendations. Information on responses to

booster doses and on co-administration with other childhood vaccines is given in sections 5.1 and 4.5, respectively. The need for booster doses in subjects primed with a single dose (i.e. aged 12 months or more when first immunised) has not yet been established (see section 5.1).

Adolescents and adults
Menjugate Kit should be administered as a single 0.5 ml injection.

Elderly
There are no data in adults aged 65 years and older (see section 5.1).

There are no data on the use of different Meningococcal group C conjugate vaccines within the primary series or for boosting. Whenever possible, the same vaccine should be used throughout.

Method of Administration
Intramuscular injection. The vaccine (0.5 ml) is intended for deep intramuscular injection, preferably in the anterolateral thigh in infants and in the deltoid region in older children, adolescents and adults.

Precautions to be taken before handling or administering the medicinal product:
The vaccine must not be injected intravenously, subcutaneously or intradermally.
Menjugate Kit must not be mixed with other vaccines in the same syringe. Separate injection sites must be used if more than one vaccine is being administered (see section 4.5).

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1, including diphtheria toxoid.

Persons who have shown signs of hypersensitivity after previous administration of Menjugate Kit.

As with other vaccines, administration of Menjugate Kit must be postponed in subjects with an acute severe febrile illness.

4.4 Special warnings and precautions for use

Before the injection of any vaccine, the person responsible for administration must take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic event following administration of the vaccine.

Prior to administration of any dose of Menjugate Kit, the parent or guardian must be asked about the personal history, family history, and recent health status of the vaccine recipient, including immunisation history, current health status and any adverse event after previous immunisations.

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions, may occur in association with vaccination as a psychogenic response to the needle injection (see section 4.8). It is important that procedures are in place to avoid injury from fainting.

The benefits of vaccination with meningococcal group C conjugate vaccine must be reviewed in light of the incidence of *N. meningitidis* group C infection in a given population before the institution of a widespread immunisation campaign.

Menjugate Kit will not protect against meningococcal diseases caused by any of the other types of meningococcal bacteria (A, B, 29-E, H, I, K, L, W-135, X, Y, or Z, including non-typed). Complete protection against meningococcal group C infection cannot be guaranteed.

No data on the applicability of the vaccine for post-exposure outbreak control are as yet available.

In individuals deficient in producing antibodies, vaccination may not result in an appropriate protective antibody response. While HIV infection is not a contraindication, Menjugate Kit has not been specifically evaluated in the immunocompromised. Individuals with complement deficiencies and individuals with functional or anatomical asplenia may mount an immune response to meningococcal group C conjugate vaccines; however, the degree of protection that would be afforded is unknown**.**

Although symptoms of meningism such as neck pain/stiffness or photophobia have been reported there is no evidence that the vaccine causes meningococcal C meningitis. Clinical alertness to the possibility of co-incidental meningitis must therefore be maintained.

Conjugate vaccines containing CRM197 should not be considered as immunising agents against diphtheria. No changes in the schedule for administering vaccines containing Diphtheria Toxoid are recommended.

Any acute infection or febrile illness is reason for delaying the use of Menjugate Kit except when, in the opinion of the physician, withholding the vaccine entails a greater risk. A minor afebrile illness, such as a mild upper respiratory infection, is not usually reason to defer immunisation.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

The vaccine must not be injected intravenously, subcutaneously or intradermally.

Menjugate Kit has not been evaluated in persons with thrombocytopenia or bleeding disorders. The risk versus benefit for persons at risk of haemorrhage following intramuscular injection must be evaluated.
Parents must be informed of the immunisation schedule for this vaccine. Precautions such as useful antipyretic measures for this vaccine must be relayed to the parent or guardian and the need to report any adverse event must be stressed.

The tip cap of the syringe may contain 10% Dry Natural Rubber. Although the risk for developing allergic latex reactions is very small, healthcare professionals are encouraged to consider the benefit risk prior to administering this vaccine to patients with known history of hypersensitivity to latex.

There are no data in adults aged 65 years and older.

4.5 Interaction with other medicinal products and other forms of interaction

Menjugate Kit must not be mixed with other vaccines in the same syringe.
If two or more vaccines need to be administered at the same time, they must be given at separate injection sites, preferably in different arms or legs.

Administration of Menjugate Kit at the same time as (but, for injected vaccines, at a different injection site) the following vaccines in clinical studies did not reduce the immunological response to any of these other antigens:
- Polio (inactivated polio vaccine [IPV] and oral polio vaccine [OPV]);
- Diphtheria [D] and Tetanus [T] toxoids alone or in combination with whole cell [wP] or acellular Pertussis [aP];
- *Haemophilus Influenzae* type B [Hib] conjugate vaccine;
- Hepatitis B [HBV] vaccine administered alone or at the same time as combined vaccine containing D, T, Hib, IPV and aP;
- Combined measles, mumps and rubella vaccine;
- 7-valent pneumococcal conjugate vaccine (Prevenar). The effect of concomitant administration of Menjugate with 7-valent pneumococcal conjugate vaccine (Prevenar) and a hexavalent vaccine [DTaP-HBV-IPV-Hib] on immune responses was assessed in infants vaccinated at median ages of approximately 2, 4.5 and 6.5 months. The potential for immune interference has not been assessed at other primary immunisation schedules.

Minor variations in GMT antibody titres were observed between studies; however, the clinical significance, if any, of these observations is not established.

In various studies with different vaccines, concomitant administration of meningococcal group C conjugates with combinations containing aP components (with or without IPV, hepatitis B surface antigen or Hib conjugates) has been shown to result in lower SBA GMTs compared to separate administrations or to co-administration with whole cell pertussis vaccines. The proportions reaching SBA titres of at least 1:8 or 1:128 are not affected. At present, the potential implications of these observations for the duration of protection are not known.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data on the use of this vaccine in pregnant women. Animal studies in rabbit at different stages of gestation have not demonstrated a risk to the foetus following administration of Menjugate Kit. Nevertheless, considering the severity of meningococcal group C disease pregnancy should not preclude vaccination when the risk of exposure is clearly defined.

Breast-feeding
Information on the safety of the vaccine during lactation is not available. The benefit-risk ratio must be examined before making the decision as to whether to immunise during lactation.

Fertility
Impairment of fertility was not evaluated in humans or in animal studies.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
Dizziness has been very rarely reported following vaccination. This may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Tabulated list of adverse reactions

Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.
Frequencies are defined as follows:

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)
Not known (cannot be estimated from the available data)

Adverse Reactions from clinical trials
Adverse reactions reported across all age groups are provided below. Adverse reactions were collected on the day of vaccination and each day following for at least 3 and up to 6 days. The majority of reactions were self-limiting and resolved within the follow-up period.

In all age groups injection site reactions (including redness, swelling and tenderness/pain) were very common (ranging from 1 in 3 older children to 1 in 10 pre-school children). However, these were not usually clinically significant. Redness or swelling of at least 3 cm and tenderness interfering with movement for more than 48 hours was infrequent where studied.

Fever of at least 38.0°C is common (ranging from 1 in 20 in infants and toddlers to 1 in 10 in pre-school children), but

does not usually exceed 39.1°C, particularly in older age groups.
In infants and toddlers symptoms including crying and vomiting (toddlers) were common after vaccination. Irritability, drowsiness, impaired sleeping, anorexia, diarrhoea and vomiting (infants) were very common after vaccination. There was no evidence that these were related to Menjugate Kit rather than concomitant vaccines, particularly DTP.

Very commonly reported adverse events include myalgia and arthralgia in adults. Drowsiness was commonly reported in younger children. Headache was very common in secondary school children and common in primary school children.

Adverse reactions reported across all age groups

General disorders and administration site conditions
Very common: Injection site reactions (redness, swelling and tenderness/pain)
Common: Fever ≥ 38.0°C

Additional reactions reported in infants (first year of life) and toddlers (second year of life)

Gastrointestinal disorders
Very common: Diarrhoea and anorexia, vomiting (infants)
Common: Vomiting (toddlers)

General disorders and administration site conditions
Very common: Irritability, drowsiness and impaired sleeping
Common: Crying

Additional reactions reported in older children and adults

Gastrointestinal disorders
Very common: Nausea (adults)

Musculoskeletal and connective tissue disorders
Very common: Myalgia and arthralgia

General disorders and administration site conditions
Very common: Malaise, headache (secondary school children)
Common: Headache (primary school children)

Adverse Reactions from Post Marketing Surveillance (for all age groups)
The most commonly reported suspected reactions in post marketing surveillance include dizziness, pyrexia, headache, nausea, vomiting and faints.

The frequencies given below are based on spontaneous reporting rates, for this and other Meningococcal group C conjugate vaccines and have been calculated using the number of reports received as the numerator and the total number of doses distributed as the denominator.

Immune system disorders
Very rare: Lymphadenopathy, anaphylaxis including anaphylactic shock, hypersensitivity reactions including bronchospasm, facial oedema and angioedema.

Nervous system disorders
Very rare: Dizziness, convulsions including febrile convulsions, faints, hypoaesthesia and paraesthesia, hypotonia

There have been very rare reports of seizures following Menjugate vaccination; individuals have usually rapidly recovered. Some of the reported seizures may have been faints. The reporting rate of seizures was below the background rate of epilepsy in children. In infants seizures were usually associated with fever and were likely to be febrile convulsions.

There have been very rare reports of visual disturbances and photophobia following vaccination with Meningococcal group C conjugate vaccines, usually in conjunction with other neurological symptoms like headache and dizziness.

Respiratory, thoracic and mediastinal disorders
Apnoea in very premature infants (≤ 28 weeks of gestation) (see section 4.4)

Gastrointestinal disorders
Very rare: Nausea, vomiting and diarrhoea

Skin and subcutaneous tissue disorders
Very rare: Rash, urticaria, pruritus, purpura, erythema multiforme and Stevens-Johnson Syndrome

Musculoskeletal and connective tissue disorders
Very rare: Myalgia and arthralgia

General disorders and administration site conditions
Very rare: Extensive swelling of the vaccinated limb

Relapse of nephrotic syndrome has been reported in association with Meningococcal group C conjugate vaccines.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: http://www.hpra.ie/; E-mail: medsafety@hpra.ie.

4.9 Overdose

No case of overdose has been reported. Since each injection is a single dose of 0.5 millilitres, overdose is unlikely.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: meningococcal vaccines, ATC code: J07AH07.

Immunogenicity
No prospective efficacy trials have been performed.

The serum bactericidal assay (BCA) referenced in the text below used human serum as a source of complement. Serum bactericidal assay (BCA) results achieved with human serum as a source of complement are not directly comparable with those achieved with rabbit serum as a source of complement.

Data on the use of a 2-dose primary immunisation series are available from a clinical trial that compared a 2, 3, 4 month vaccination schedule to a 2, 4 month vaccination schedule in 241 infants. One month after completion of the primary series nearly all subjects had attained hBCA titres ≥ 1:8 (100% and 98% in respective groups). At 28 days after a challenge dose of unconjugated MenC vaccine at 12 months of age, all of 50 subjects primed with three doses and 54/56 (96%) primed with two doses achieved hBCA titres ≥ 1:8.

Compared to licensed unconjugated meningococcal polysaccharide vaccines in clinical studies, the immune response induced by Menjugate Kit was shown to be superior in toddlers, children and adolescents, and was comparable in adults (see table). Additionally, unlike unconjugated polysaccharide vaccines, Menjugate Kit induces immunologic memory after vaccination, although the duration of protection is not yet established.

There are no data in adults aged 65 years or older.

Comparison of the Percentage of Subjects with Antimeningococcal C Serum Bactericidal Titres ≥1:8 (Human Complement) at One Month Following One Immunization of Menjugate or a Licensed Unconjugated Meningococcal Polysaccharide Vaccine, by Age Group at Enrolment								
	Age 1-2 years		Age 3-5 years		Age 11-17 years		Age 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
BCA % ≥1:8 (95% CI) Human Complement	78% (72-83)	19% (13-26)	79% (68-87)	28% (18-39)	84% (75-91)	68% (57-77)	90% (84-95)	88% (82-93)

MenPS = licensed unconjugated Meningococcal polysaccharide vaccine.
(1) = groups A, C, W-135 and Y, containing 50µg of group C per dose.
(2) = groups A and C, containing 50µg of group C per dose.

No pharmacodynamic studies have been conducted with Menjugate Kit, in accordance with its status as a vaccine.

Post-marketing surveillance following an immunisation campaign in the UK
Estimates of vaccine effectiveness from the UK's routine immunisation programme (using various quantities of three meningococcal group C conjugate vaccines) covering the period from introduction at the end of 1999 to March 2004 demonstrated the need for a booster dose after completion of the primary series (three doses administered at 2, 3 and 4 months). Within one year of completion of the primary series, vaccine effectiveness in the infant cohort was estimated at 93% (95% confidence intervals 67, 99). However, more than one year after completion of the primary series, there was clear evidence of waning protection.
Up to 2007 the overall estimates of effectiveness in age cohorts from 1-18 years that received a single dose of meningococcal group C conjugate vaccine during the initial catch-up vaccination programme in the UK fall between 83 and 100%. The data show no significant fall in effectiveness within these age cohorts when comparing time periods less than a year or one year or more since immunisation.

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been conducted with Menjugate Kit, in accordance with its status as a vaccine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity to reproduction (embryofetal studies).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial containing MenC-CRM197 Conjugate
- Mannitol
- Sodium dihydrogen phosphate monohydrate
- Disodium phosphate – heptahydrate

Syringe containing aluminium hydroxide
- Sodium chloride
- Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

Following reconstitution, the product should be used immediately.

The two components of the product may have different expiry dates. The outer carton bears the earlier of the two dates and this date must be respected. The carton and ALL its contents must be discarded on reaching this outer carton expiry date.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze. Keep the vial and the syringe in the outer carton in order to protect from light

6.5 Nature and contents of container

Menjugate Kit is presented as a vial of powder (type I glass), with a stopper (bromobutyl rubber) and 0.6 ml of solvent in a syringe (type I glass) with a stopper (bromobutyl rubber) and a tip cap (either chlorobutyl rubber or styrene butadiene rubber) - pack sizes of 1, 5 or 10 single doses.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The lyophilised vaccine will require preparation by reconstitution with aluminium hydroxide solvent.

Gently agitate the syringe containing the aluminium hydroxide solvent. Remove the tip cap from the syringe and attach a suitable needle. Use the whole content of the syringe (0.6 ml of suspension) to reconstitute the Meningococcal group C conjugate vaccine vial. Gently shake the reconstituted vial until the vaccine is dissolved (this will ensure the antigen is bound to the adjuvant). Taking care not to withdraw the plunger completely out of the barrel of the syringe, withdraw the full contents of the vial into the syringe. Please note that it is normal for a small residual amount of liquid to remain in the vial following withdrawal of the dose. Please ensure that no air bubbles are present in the syringe before injecting the vaccine.

Following reconstitution the vaccine is a slightly opaque, colourless to light yellow suspension, free from visible foreign particles. In the event of any foreign particulate matter and/or variation of physical aspect being observed, discard the vaccine.

Any unused product or waste material should be disposed in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

GSK Vaccines S.r.l.
Via Fiorentina 1
53100 Siena
Italy

8 MARKETING AUTHORISATION NUMBER

PA 0919/004/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 April 2005

Date of last renewal: 01 March 2010

10 DATE OF REVISION OF THE TEXT

January 2018