

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MENJUGATE 10 micrograms suspension for injection

Meningococcal group C conjugate vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

<i>Neisseria meningitidis</i> group C (strain C11) oligosaccharide conjugated to	10 micrograms
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<i>Corynebacterium diphtheriae</i> CRM197 protein ¹ adsorbed on aluminium hydroxide	12.5 to 25.0 micrograms 0.3 to 0.4 mg Al ³⁺
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¹CRM197 (Cross Reacting Material 197)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.

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 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 with other vaccines).

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

The safety and efficacy of Menjugate 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 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 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 handling of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients of the vaccine listed in section 6.1, including diphtheria toxoid (CRM197), or a life-threatening reaction after previous administration of a vaccine containing similar components (see section 4.4).

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.

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.

Menjugate will not protect against meningococcal diseases caused by any of the other types of meningococcal bacteria. Complete protection against meningococcal group C infection cannot be guaranteed.

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

In individuals deficient in producing antibodies, vaccination may not result in an appropriate protective antibody response. Menjugate has not been specifically evaluated in the immunocompromised. Individuals with HIV infection, 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.

Individuals with familial complement deficiencies (for example, C3 or C5 deficiencies) and individuals receiving treatments that inhibit terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* group C, even if they develop antibodies following vaccination with Menjugate.

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 except when, in the opinion of the physician, withholding the vaccine entails a greater risk. A minor infection or minor febrile illness 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 $\leq$ 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 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.

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

Latex-sensitive individuals

Although no natural rubber latex is detected in the syringe tip cap, the safe use of Menjugate in latex-sensitive individuals has not been established.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Menjugate 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 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. 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 breast-feeding.

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 ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ 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 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 $\geq 38.0^\circ\text{C}$

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)

The safety of Menjugate liquid formulation was compared with that of Menjugate lyophilised formulation in a randomised clinical study involving 989 children aged 12 months to 2 years. The safety profile of both formulations of Menjugate was comparable.

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: 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 activity (SBA) referenced in the text below used human serum as a source of complement. Serum bactericidal activity (SBA) 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 with the lyophilised formulation 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 hSBA titres $\geq 1:8$ (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 hSBA titres $\geq 1:8$.

Compared to licensed unconjugated meningococcal polysaccharide vaccines in clinical studies, the immune response induced by Menjugate lyophilised formulation was shown to be superior in toddlers, children and adolescents, and was comparable in adults (see table). Additionally, unlike unconjugated polysaccharide vaccines, Menjugate 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 $\geq 1:8$ (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
SBA % ≥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.

In a randomised clinical study involving 989 children aged 12 months to 2 years the immunogenicity of Menjugate liquid formulation was compared with that of Menjugate lyophilised formulation produced with active substance from two different manufacturing sites. For Menjugate liquid formulation, geometric mean titers (GMT) were 4.69 (4.01-5.49); for Menjugate lyophilised formulation GMT were 5.6 (4.79-6.54) and 6.34 (5.4-7.45). The antibody response induced by both formulations of Menjugate was comparable. This was demonstrated by the two-sided 95% CI for the corresponding vaccine group GMT ratios falling within the predefined equivalence interval (0.5 - 2.0) 28 days post-vaccination. At the same time point, the proportion of subjects with hSBA ≥1:8 were 60% (54-65) for the liquid formulation, 63% (57-69) and 70% (64-76) for the lyophilised formulation. These results were consistent with the pooled rate observed in toddlers in previous studies (63%, CI 60-67) with Menjugate lyophilised formulation.

There are no data in children 2-12 months of age with liquid formulation.

No pharmacodynamic studies have been conducted with Menjugate, 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, 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 (embryo/fetal studies).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Histidine
- Sodium chloride
- Water for injection

For adsorbant see Section 2.

6.2 Incompatibilities

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

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze. Keep the syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

Menjugate is presented as:

A syringe (type I glass) with stopper (bromobutyl rubber) and tip cap (styrene butadiene type II rubber), filled with 0.6 ml of vaccine.

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

Gently shake the syringe containing the vaccine before administration. Remove the syringe tip cap and fit a suitable needle. The vaccine should be visually inspected for particulate matter and discoloration prior to administration. Ensure that no air bubbles are present in the syringe before injecting the vaccine. 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 of 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 0919/004/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08/05/2015

Date of latest renewal: 08/01/2020

10. DATE OF REVISION OF THE TEXT

28 September 2021