**WHO LEAFLET**

## DESCRIPTION

***Nimenrix™*** powder and solvent for solution for injection
Meningococcal polysaccharide serogroups A, C, W-135, and Y conjugate vaccine

After reconstitution, 1 dose (0.5 ml) contains 5 micrograms of *Neisseria meningitidis* polysaccharide for serogroups A[1], C[1], W-135[1], and Y[1].
[1]conjugated to 44 micrograms of tetanus toxoid carrier protein.
Excipients:
Powder: sucrose, trometamol
Solvent: sodium chloride, water for injections

## ADMINISTRATION

***Nimenrix™*** is for intramuscular injection only, preferably into the deltoid muscle.
In infants, the recommended injection site is the anterolateral aspect of the thigh. In individuals from 1 year of age, the recommended injection site is the anterolateral aspect of the thigh or the deltoid muscle.

See also sections *Immunization Schedule* and *Precautions.*

The powder of ***Nimenrix™*** is a white powder or cake and the solvent is clear and colourless solution. Solvent must be cooled between 2°C and 8°C before used for reconstitution.

***Nimenrix™*** must be reconstituted by adding the entire contents of the vial of solvent to the vial containing the powder.

1 Withdraw the entire contents of the solvent vial and add the solvent to the powder vial.
2 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.
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.

According to WHO recommendations, once the vaccine has been reconstituted, it should be maintained between +2°C to +8°C and protected from the sunlight; the vial must be discarded at the end of each immunisation session or after 6 hours from reconstitution, whichever comes first.

## IMMUNIZATION SCHEDULE

***Nimenrix™*** is used for active immunization of individuals from 6 weeks of age against invasive meningococcal diseases caused by *Neisseria meningitidis* serogroups A, C, W-135, and Y (see section *Pharmacological properties*).

### *Vaccination schedule*

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

Infants from 6 weeks to less than 6 months of age
Your child should receive an initial course of 2 injections of the vaccine followed by a booster.
- The first injection should be given from 6 weeks of age. There should be an interval of 2 months between the first and second injections.
- A third injection (booster) should be given at 12 months.

Unvaccinated Infants from 6 months to less than 12 months of age
Your child should receive one injection followed by a booster.
- The first injection should be given from 6 months of age.
- A second injection (booster) should be given at 12 months of age with a minimum interval of at least 2 months after the first injection.

Children from 12 months of age, adolescents and adults
You or your child should receive one injection.

Please tell your doctor if you have received a previous injection with another meningococcal vaccine than ***Nimenrix™***.

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

Your doctor will tell you if and when you need an additional dose of ***Nimenrix™***, especially if you or your child:

- received your first dose at age 6-14 months and could be at particular risk of infection caused by *Neisseria meningitidis* types W-135 and Y
- received your dose more than approximately one year ago and could be at risk of infection caused by *Neisseria meningitidis* type A
- received your first dose at age 12-23 months and could be at particular risk of infection caused by *Neisseria meningitidis* types A, C, W-135 and Y

You will be informed when you or your child should come back for the next injection. If you or your child misses a scheduled injection, it is important that you make another appointment.

Make sure you or your child finishes the complete vaccination course.

***Use with other vaccines or medicinal products***

In infants, ***Nimenrix™*** can be given concomitantly with combined DTaP-HBV-IPV/Hib vaccines and with 10-valent pneumococcal conjugate vaccine.

From age 1 year and above, ***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.

In the first two years of life, ***Nimenrix™*** can also be given concomitantly with combined diphtheria - tetanus - acellular pertussis (DTaP) vaccines, including combination DTaP vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b (HBV, IPV or Hib), such as DTaP-HBV-IPV/Hib vaccine and 13-valent pneumococcal conjugate vaccine.

In individuals aged 9 to 25 years, ***Nimenrix™*** can be given concomitantly with human papillomavirus vaccine [Type 16 and 18] and a combined diphtheria (reduced antigen content), tetanus and acellular pertussis vaccine.

Whenever possible, ***Nimenrix™*** and a 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.

The safety and immunogenicity of ***Nimenrix™*** was evaluated when it was sequentially administered or co-administered with a vaccine containing diphtheria and tetanus toxoids, acellular pertussis, inactivated polioviruses (1, 2 and 3), hepatitis B surface antigen and *Haemophilus influenza* type b polyribosyl ribose phosphate conjugated to tetanus toxoid (DTaP-HBV-IPV/Hib) in the second year of life. The administration of ***Nimenrix™*** one month after the DTaP-HBV-IPV/Hib vaccine resulted in lower rSBA GMTs against groups A, C and W-135, compared with co-administration.

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). The clinical relevance of this observation is unknown. There was no impact of co-administration on immune responses to 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.

## SIDE EFFECTS

The safety profile presented below is based on a pooled analysis in more than 10,000 subjects who have been vaccinated with one dose of ***Nimenrix™*** in clinical studies.

Side effects reported are listed according to the following frequency:

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)

| **System Organ Class** | **Frequency** | **Side effects** |
|---|---|---|
| Blood and lymphatic system disorders | Not known*** | Lymphadenopathy |
| Metabolism and nutrition disorders | Very common | Appetite lost |
| Psychiatric disorders | Very common | Irritability |
| | Uncommon | Insomnia<br>Crying |
| Nervous system disorders | Very common | Drowsiness<br>Headache |
| | Uncommon | Hypoaesthesia<br>Dizziness |
| | Rare | Febrile convulsion |

| System Organ Class | Frequency | Side effects |
|---|---|---|
| Gastrointestinal disorders | Common | Diarrhoea<br>Vomiting<br>Nausea* |
| Skin and subcutaneous tissue disorders | Uncommon | Pruritus<br>Urticaria<br>Rash** |
| Musculoskeletal and connective tissue disorders | Uncommon | Myalgia<br>Pain in extremity |
| General disorders and administration site conditions | Very common | Fever<br>Swelling at injection site<br>Pain at injection site<br>Redness at injection site<br>Fatigue |
| | Common | Injection site haematoma* |
| | Uncommon | Malaise<br>Injection site induration<br>Injection site pruritus<br>Injection site warmth<br>Injection site anaesthesia |
| | Not known*** | Extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb |

*Nausea and Injection site haematoma occurred at a frequency of Uncommon in infants
**Rash occurred at a frequency of Common in infants
***ADR identified post-marketing

## 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.

Intercurrent illness
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
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.

Thrombocytopenia and coagulation disorders
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.

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

Protection against meningococcal disease
***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.

*Effect of prior vaccination with plain polysaccharide meningococcal vaccine*

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 a serum bactericidal assay using rabbit complement (rSBA) than subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years (see section *Pharmacological properties*). The clinical relevance of this observation is unknown.

*Immune response in infants aged 6 months to less than 12 months*

A single dose administered at 6 months was associated with lower human complement serum bactericidal assay (hSBA) titres to groups W-135 and Y compared with three doses administered at 2, 4, and 6 months (see section *Pharmacological properties*). The clinical relevance of this observation is unknown. If an infant aged 6 months to less than 12 months is expected to be at particular risk of invasive meningococcal disease due to exposure to groups W-135 and/or Y, consideration may be given to administering a second primary dose of ***Nimenrix™*** after an interval of 2 months.

*Immune responses in toddlers aged 12-14 months*

Toddlers aged 12-14 months had similar rSBA titres to groups A, C, W-135, and Y at one month after one dose of ***Nimenrix™*** or at one month after two doses of ***Nimenrix™*** given two months apart.

A single dose was associated with lower hSBA titres to groups W-135, and Y compared with two doses given two months apart. Similar responses to groups A and C were observed after one or two doses (see section *Pharmacological properties*). The clinical relevance of this observation is unknown. If a toddler is expected to be at particular risk of invasive meningococcal disease due to exposure to groups W-135, and/or Y, consideration may be given to administering a second dose of ***Nimenrix™*** after an interval of 2 months. Regarding waning of antibody against group A or group C after a first dose of ***Nimenrix™*** in children aged 12-23 months, see under *Persistence of serum bactericidal antibody titres*.

Persistence of serum bactericidal antibody titres

Following administration of ***Nimenrix™*** there is a waning of serum bactericidal antibody titres against group A when using hSBA (see section *Pharmacological properties*). The clinical relevance of this observation is unknown. However, if an individual is expected to be at particular risk of exposure to group A and received a dose of ***Nimenrix™*** more than approximately one year previously, consideration may be given to administering a booster dose.

A decline in antibody titres over time has been observed for groups A, C, W-135, and Y. The clinical relevance of this observation is unknown. A booster dose might be considered in individuals vaccinated at toddler age remaining at high risk of exposure to meningococcal disease caused by groups A, C, W-135, or Y (see section *Pharmacodynamic properties*).

Effect of ***Nimenrix™*** on anti-tetanus antibody concentrations

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

Giving ***Nimenrix™*** with or one month before a TT-containing vaccine in the second year of life does not impair the response to TT or significantly affect safety. No data are available beyond the age of 2 years.

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

***Preclinical 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.

***Incompatibilities***

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

## PHARMACOLOGICAL PROPERTIES

For this section, see WHO Product Information on the WHO website.

## STORAGE

The expiry date is indicated on the label and packaging.

Store in a refrigerator (2°C – 8°C).
The solvent may also be stored at ambient temperature (30°C). Solvent must be cooled between +2°C and +8°C before reconstitution.
Do not freeze.
Protect from light.

## PRESENTATION

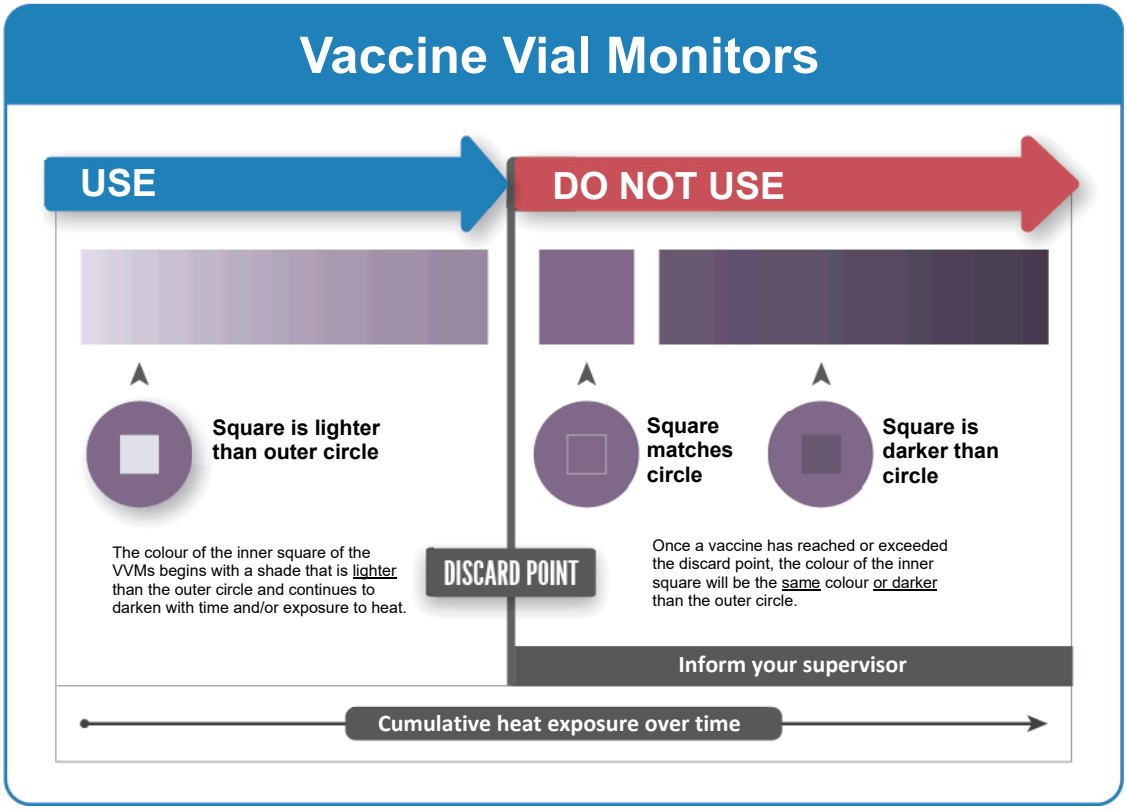
Powder in a vial containing 1 dose (type I glass) with a stopper (butyl rubber) and 0.5 ml of solvent for 1 dose in a vial (type I glass).
Pack size of 50

### Vaccine Vial Monitor (see VVM pictogram at the end of the leaflet)

The Vaccine Vial Monitor (VVM) is part of the cap used for all ***Nimenrix*™** batches supplied by Pfizer Limited. The colour dot that appears on the cap of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

It is absolutely critical to ensure that the storage conditions specified above (in particular the cold chain) are complied with. Pfizer Limited will assume no liability in the event ***Nimenrix*™** has not been stored in compliance with the storage instructions. Furthermore Pfizer Limited assumes no responsibility in case a VVM is defective for any reason.

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