SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

COVAXiS, suspension for injection.

Diphtheria, Tetanus, Pertussis (acellular component) Vaccine (adsorbed, reduced antigen(s) content)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Diphtheria Toxoid	Not less than 2 IU* (2 Lf)
Tetanus Toxoid	Not less than 20 IU* (5 Lf)
Pertussis Antigens	
Pertussis Toxoid	2.5 micrograms
Filamentous Haemagglutinin	5 micrograms
Pertactin	3 micrograms
Fimbriae Types 2 and 3	5 micrograms
Adsorbed on aluminium phosphate	1.5 mg (0.33 mg aluminium)

* As lower confidence limit (p = 0.95) of activity measured according to the assay described in the European Pharmacopoeia.

This vaccine may contain traces of formaldehyde and glutaraldehyde which are used during the manufacturing process (see sections 4.3 and 4.4).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection

COVAXiS appears as a cloudy white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

COVAXiS is indicated for active immunization against tetanus, diphtheria and pertussis in persons from 4 years of age as a booster following primary immunization.

The use of COVAXiS should be determined on the basis of official recommendations.

4.2 Posology and method of administration

Posology

A single injection of one (0.5 mL) dose is recommended in all indicated age groups.

COVAXiS is a vaccine containing low-dose diphtheria-, tetanus- and pertussis-antigens indicated for booster vaccinations. When administering the vaccine, indications and dosing intervals according to the official recommendations should be considered for all antigens contained in the vaccine.

Individuals with an incomplete, or no history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with COVAXiS.

COVAXiS is not precluded in persons with an incomplete, or no history of previous pertussis vaccination. However, a booster response will only be elicited in individuals who have been previously primed by vaccination or by natural infection.

COVAXiS can be used for repeat vaccination to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 year intervals (see section 5.1). Repeat vaccination should be performed according to official recommendations.

COVAXiS can be used in the management of tetanus prone injuries with or without concomitant administration of Tetanus Immunoglobulin according to official recommendations.

Paediatric population

Children from the age of 4 years onwards and adolescents should receive the same dosage as adults.

Method of administration

A single injection of one dose (0.5 mL) of COVAXiS should be administered intramuscularly. The preferred site is into the deltoid muscle.

COVAXiS should not be administered into the gluteal area; intradermal or subcutaneous routes should not be used (in exceptional cases the subcutaneous route may be considered, see section 4.4).

Precautions to be taken before handling or administering the medicinal product

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

4.3 Contraindications

- COVAXiS should not be administered to person with known hypersensitivity
  - to diphtheria, tetanus or pertussis vaccines
  - to any other component of the vaccine (see section 6.1)
  - to any residual substances carried over from manufacture (formaldehyde and glutaraldehyde), which may be present in undetectable trace amounts.
- COVAXiS should not be administered to persons who experienced an encephalopathy of unknown origin within 7 days of previous immunization with a pertussis-containing vaccine.
- As with other vaccines, COVAXiS should be postponed in persons suffering from an acute severe febrile illness. The presence of a minor infection is not a contraindication.

4.4 Special warnings and precautions for use

COVAXiS should not be used for primary immunization.

Regarding the interval between a booster dose of COVAXiS and preceding booster doses of diphtheria and/or tetanus containing vaccines, the official recommendations should generally be followed. Clinical data have demonstrated that there was no clinically relevant difference in rates of adverse reactions associated with administration of a tetanus-, diphtheria- and pertussis-containing booster vaccine as early as 4 weeks, compared to at least 5 years, after a preceding dose of tetanus and diphtheria-containing vaccine.

Prior to immunization

Vaccination should be preceded by a review of the person's medical history (in particular previous vaccinations and possible adverse events). In persons who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, administration of COVAXiS vaccine must be carefully considered.

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

If Guillain-Barré syndrome or brachial neuritis has occurred following receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

COVAXiS should not be administered to persons with progressive neurological disorder, uncontrolled epilepsy or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized.

The immunogenicity of the vaccine could be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone the vaccination until the end of such disease or treatment if practical. Nevertheless, vaccination of HIV infected persons or persons with chronic immunodeficiency, such as AIDS, is recommended even if the antibody response might be limited.

Administration precautions

Do not administer by intravascular or intradermal injection.

Intramuscular injections should be given with care in patients on anticoagulant therapy or suffering from coagulation disorders because of the risk of haemorrhage. In these situations administration of COVAXiS by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

Other considerations

As with any vaccine, vaccination with COVAXiS may not protect 100% of susceptible individuals.

A persistent nodule at the site of injection may occur with all adsorbed vaccines particularly if administered into the superficial layers of the subcutaneous tissue.

4.5 Interaction with other medicinal products and other forms of interaction

Based on the results of concomitant use clinical studies, COVAXiS can be administered concomitantly with any of the following vaccines: inactivated Influenza vaccine, Hepatitis B vaccine, Inactivated or Oral Poliomyelitis vaccine and recombinant Human Papillomavirus vaccine (See section 4.8) according to local recommendations.

Separate limbs must be used for the site of injection of concomitant parenteral vaccines. Interaction studies have not been carried out with other vaccines, biological products, or therapeutic medications. However, in accordance with commonly accepted immunization guidelines, since COVAXiS is an inactivated product it may be administered concomitantly with other vaccines or immunoglobulins at a separate injection site.

In the case of immunosuppressive therapy please refer to section 4.4.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a limited number of exposed pregnancies indicated no adverse effect of COVAXiS on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

COVAXiS should be given to a pregnant woman only if clearly needed, based on an assessment of the benefits versus the risks.

Breast-feeding

It is not known whether the active substances included in COVAXiS are excreted in human milk but antibodies to the vaccine antigens have been found to be transferred to the suckling offspring of rabbits. An animal developmental study conducted in rabbits has not shown any harmful effects of maternal antibodies induced by the vaccine on offspring postnatal development.

However, the effect on breast-fed infants of the administration of COVAXiS to their mothers has not been studied. The risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.

Fertility

COVAXiS has not been evaluated in fertility studies.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed. COVAXiS has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

In clinical trials COVAXiS was given to a total of 4,546 persons, including 298 children (4 to 6 years), 1,313 adolescents (11 to 17 years) and 2,935 adults (18 to 64 years). Most commonly reported reactions

following vaccination included local reactions at the injection site (pain, redness and swelling) that occurred in 21% - 78% of the vaccinees, headache and tiredness that occurred in 16% - 44% of vaccinees. These signs and symptoms usually were mild in intensity and occurred within 48 hours following vaccination. They all resolved without sequelae.

Safety analysis was conducted in 1,042 healthy adolescent males and females aged 10 to 17 years during a clinical trial. They received quadrivalent human papillomavirus types 6/11/16/18 vaccine (Gardasil) concurrently with a dose of COVAXiS and a dose of quadrivalent meningococcal conjugate vaccine serogroup A, C, Y and W135. The safety profiles were similar in both concomitant and non concomitant groups. Higher frequencies of swelling at the Gardasil injection site, bruising and pain at COVAXiS injection sites were observed in the concomitant administration group. The differences observed between concomitant and non concomitant groups were less than 7% and in a majority of subjects the adverse events were reported as mild to moderate in intensity.

Tabulated list of adverse reactions

Adverse reactions are ranked under headings of frequency using the following convention:

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

Table 1 presents adverse reactions observed in clinical trials and also includes additional adverse events which have been spontaneously reported during the post-marketing use of COVAXiS worldwide. Because post-marketing adverse events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Therefore, the frequency category “Not known” is assigned to these adverse events.

Table 1: Adverse events from trials and worldwide post-marketing experience

System Organ Class	Frequency	Children (4 to 6 Years)	Adolescents (11 to 17 Years)	Adults (18 to 64 Years)
Immune system disorders	Not known	Hypersensitivity (Anaphylactic) reaction (Angioedema, Oedema, Rash, Hypotension)*		
Metabolism and nutrition disorders	Very common	Anorexia (decreased appetite)		
Nervous system disorders	Very common	Headache		
	Not known	Paraesthesia*, Hypoaesthesia*, Guillain-Barré Syndrome*, Brachial Neuritis*, Facial Palsy*, Convulsions*, Syncope*, Myelitis*		
Cardiac disorders	Not known	Myocarditis*		
Gastrointestinal disorders	Very common	Diarrhoea	Diarrhoea, Nausea	Diarrhoea
	Common	Nausea, Vomiting	Vomiting	Nausea, Vomiting

System Organ Class	Frequency	Children (4 to 6 Years)	Adolescents (11 to 17 Years)	Adults (18 to 64 Years)
Skin and subcutaneous system disorders	Common	Rash		
	Not known	Pruritus*, Urticaria*		
Musculoskeletal and connective tissue disorders	Very common		Generalized aching or Muscular weakness, Arthralgia or Joint swelling	Generalized aching or Muscular weakness
	Common	Generalized aching or Muscular weakness, Arthralgia or Joint swelling		Arthralgia or Joint swelling
	Not known	Myositis*		
General disorders and administrative site conditions	Very common	Fatigue/Asthenia	Fatigue/Asthenia, Malaise, Chills	Fatigue/Asthenia, Malaise
		Injection site pain, Injection site erythema, Injection site swelling		
	Common	Pyrexia, Chills, Axillary adenopathy	Pyrexia, Axillary adenopathy	Pyrexia, Chills, Axillary adenopathy
	Not known	Injection site bruising*, Injection site sterile abscess*		

* Post-marketing Adverse Events

Description of selected adverse reactions

General Disorders and Administration Site Conditions:

Large injection site reactions (>50 mm), including extensive limb swelling from the injection site beyond one or both joints occur after administration of COVAXiS in adolescents and adults. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 - 5 days.

Paediatric population

The safety profile of COVAXiS as presented in Table 1 includes data from a clinical trial in 298 children 4 to 6 years of age who had previously received a total of 4 doses, including primary immunization, with DTaP-IPV combined with Hib, at approximately 2, 4, 6 and 18 months of age. In this clinical study, the most common adverse events reported within 14 days post-vaccination were pain at the injection site (in 39.6 % of subjects) and tiredness (in 31.5% of subjects).

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 the national reporting system listed in Appendix V.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pertussis, purified antigen, combination with toxoids.
ATC code: J07AJ52

Clinical trials

The immune responses observed one month after vaccination with COVAXiS in 265 children, 527 adolescents and 743 adults are shown in the table below.

Table 2: Immune response of children, adolescents and adults one month after vaccination with COVAXiS

Antigen	Immune Response	Children (4 to 6 Years) 265 Persons %	Adolescents (11 to 17 Years) 527 Persons %	Adults (18 to 64 Years) 743 Persons %
Diphtheria toxoid	≥0.1 IU/mL	100.0	99.8	94.1
Tetanus toxoid	≥0.1 IU/mL	100.0	100.0	100.0
Pertussis toxoid	Booster Response*	91.9	92.0	84.4
Filamentous haemagglutinin		88.1	85.6	82.7
Pertactin		94.6	94.5	93.8
Fimbriae Types 2 and 3		94.3	94.9	85.9

* For children 4-6 years of age previously primed with DTaP (diphtheria toxoid [paediatric dose], tetanus and acellular pertussis) at 2, 4, 6 and 18 months of age, a booster response is defined as a 4-fold increase in concentration of anti-pertussis antibodies.
For adolescents and adults, a booster response is defined as a 2-fold increase in concentration of anti-pertussis antibodies in participants with high pre-vaccination concentration and a 4-fold increase in participants with low pre-vaccination concentration.

The safety and immunogenicity of COVAXiS in adults and adolescents was shown to be comparable to that observed with a single dose of an adult formulation diphtheria-tetanus (Td) adsorbed vaccine containing the same amount of tetanus and diphtheria toxoids.

Serological correlates for protection against pertussis have not been established. On comparison with data from the Sweden I pertussis efficacy trials conducted between 1992 and 1996, where primary immunization with Sanofi Pasteur Limited's acellular pertussis infant DTaP formulation confirmed a protective efficacy of 85% against pertussis disease, it is considered that COVAXiS had elicited protective immune responses. The pertussis antibody levels for all antigens following a booster dose of COVAXiS in adolescents and adults exceeded those observed in a household contact study nested within the efficacy trial.

Table 3: Ratio of pertussis antibody GMCs observed one month after a dose of COVAXiS in adolescents and adults compared with those observed in infants one month following vaccination at 2, 4 and 6 months of age in the Sweden I efficacy trial with DTaP**

	Adolescents	**Adults**
	COVAXiS*/DTaP† GMCs Ratio (95% CIs)	**COVAXiS‡/DTaP† GMCs Ratio (95% CIs)**
Anti-PT	3.6 (2.8, 4.5)§	2.1 (1.6, 2.7)§
Anti-FHA	5.4 (4.5, 6.5)§	4.8 (3.9, 5.9)§
Anti-PRN	3.2 (2.5, 4.1)§	3.2 (2.3, 4.4)§
Anti-FIM	5.3 (3.9, 7.1)§	2.5 (1.8, 3.5)§

* N = 524 to 526, number of adolescents in the per-protocol population with available data for COVAXiS.

† N = 80, number of infants who received DTaP at 2, 4 and 6 months of age with available data post-dose 3 (sera from the Sweden I Efficacy Trial tested contemporaneously with samples from Clinical Trial Td506).

‡ N = 741, number of adults in the per-protocol population with available data for COVAXiS.

§ GMCs following COVAXiS were non-inferior to GMCs following DTaP (lower limit of 95% CI on the ratio of GMCs for COVAXiS divided by DTaP >0.67).

** Antibody GMCs, measured in ELISA units were calculated separately for infants, adolescents and adults.

Antibody persistence

Serology follow-up studies were conducted at 3, 5 and 10 years, in individuals previously immunized with a single booster dose of COVAXiS. Persistence of seroprotection to diphtheria and tetanus, and seropositivity to pertussis is summarised in Table 4.

Table 4: Persistence of Seroprotection/Seropositivity Rates ~~to Diphtheria and Tetanus~~ in Children, Adolescents and Adults at 3-, 5- and 10- years following a dose of COVAXiS (PPI Population*[1])

		Children (4-6 years)[2]	Adolescents (11-17 years)[2]			Adults (18-64 years)[2]		
Time point		**5 years**	**3 years**	**5 years**	**10 years**	**3 years**	**5 years**	**10 years**
Antibody		N=128-150	N=300	N=204-206	N=28-39	N=292	N=237-238	N=120-136
Diphtheria (SN, IU/mL)	≥ 0.1	86.0	97.0	95.1	94.9	81.2	81.1	84.6
	≥ 0.01	100.0	100.0	100.0	100.0	95.2	93.7	99.3
Tetanus (ELISA, IU/mL)	≥ 0.1	97.3	100.0	100.0	100.0	99.0	97.1	100.0
Pertussis (ELISA, IU/mL)	Sero-positivity[3]							
PT		63.3	97.3	85.4	82.1	94.2	89.1	85.8
FHA		97.3	100.0	99.5	100.0	99.3	100.0	100.0
PRN		95.3	99.7	98.5	100.0	98.6	97.1	99.3
FIM		98.7	98.3	99.5	100.0	93.5	99.6	98.5

N = number of subjects with available data; SN: seroneutralisation; ELISA: Enzyme Linked Immunoassay
*[1]Eligible subjects for whom immunogenicity data was available for at least one antigen at the specified time-point.
[2]Age at which subjects received a dose of COVAXiS
[3]Percentage of subjects with antibodies ≥ 4 EU/mL for PT, FHA and PRN, and ≥ 17 EU/mL for FIM for the 3 year follow-up; ≥ 4 EU/mL for PT, FIM and PRN, and ≥ 3 EU/mL for FHA for the 5-year and 10-year follow-up

~~Seropositivity to pertussis antigens – defined as an antibody concentration ≥ the lower limit of quantitation (LLOQ) – was maintained 5 years later in 63% to 99% of children, and 10 years later in 82% to 100% of adolescents / adults. (The LLOQ was ≥ 4 EU/mL for antibodies to PT, PRN and FIM, and ≥ 3 EU/mL for antibody to FHA.)~~

Immunogenicity following repeat vaccination

The immunogenicity of COVAXiS following repeat vaccination 10 years after a previous dose of COVAXiS or REPEVAX (Tdap-IPV; containing the Tdap component of COVAXiS), has been evaluated. One month post-vaccination ≥ 98.5% of study participants achieved seroprotective antibody levels (≥ 0.1 IU/ml) for diphtheria and tetanus, and ≥ 84% achieved booster responses to the pertussis antigens. (A pertussis booster response was defined as a post-vaccination antibody concentration ≥ 4 times the LLOQ if the pre-vaccination level was < LLOQ; ≥ 4 times the pre-vaccination level if that was ≥ LLOQ but < 4 times LLOQ; or ≥ 2 times the pre-vaccination level if that was ≥ 4 times the LLOQ).

Based on the serology follow-up and repeat vaccination data, COVAXiS can be used instead of a dT vaccine to boost immunity to pertussis in addition to diphtheria and tetanus.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity in pregnancy, embryonal/foetal development, parturition and postnatal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenoxyethanol
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator at 2°C to 8°C.
Do not freeze. Discard the vaccine if it has been frozen.
Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 mL suspension for injection in a vial (type I glass) with a stopper (elastomer) and seal (aluminium) with a plastic flip-off cap.

Pack sizes of 1 or 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use

Parenteral products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. In the event of either being observed, discard the medicinal product.

The normal appearance of the vaccine is a uniform, cloudy, white suspension which may sediment during storage. Shake the vial well to uniformly distribute the suspension before administering the vaccine.

When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place.

Disposal

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

Needles should not be recapped.

7 MARKETING AUTHORIZATION HOLDER

[To be completed nationally.]

8 MARKETING AUTHORIZATION NUMBER(S)

[To be completed nationally.]

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

[To be completed nationally.]

10 DATE OF REVISION OF THE TEXT

{month YYYY}.

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton – Vial Presentation

1. NAME OF THE MEDICINAL PRODUCT

COVAXiS, suspension for injection

Diphtheria, Tetanus, Pertussis (acellular, component) Vaccine (adsorbed, reduced antigen(s) content)

[NAME TO BE COMPLETED NATIONALLY]

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 mL) contains:
≥ 2 IU (2 Lf) diphtheria toxoid, ≥ 20 IU (5 Lf) tetanus toxoid, 2.5 µg pertussis toxoid, 5 µg filamentous haemagglutinin, 3 µg pertactin, 5 µg fimbriae types 2 and 3; adsorbed on 1.5 mg aluminium phosphate (0.33 mg Al).

3. LIST OF EXCIPIENTS

Excipients: Phenoxyethanol, Water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 vial
1 dose (0.5 mL)
10 vials
10 x 1 dose (0.5 mL)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Shake well before use.

Intramuscular use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

[Not applicable]

[TO BE COMPLETED NATIONALLY]

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the vials in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[TO BE COMPLETED NATIONALLY]

12. MARKETING AUTHORISATION NUMBER(S)

[TO BE COMPLETED NATIONALLY]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

[Not applicable]

16. INFORMATION IN BRAILLE

[Not applicable]

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label – Vial Presentation

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

COVAXIS, suspension for injection
dTap
I.M.
[NAME TO BE COMPLETED NATIONALLY]

2. METHOD OF ADMINISTRATION

[Not applicable]

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Sanofi Pasteur MSD or Sanofi Pasteur
[TO BE COMPLETED NATIONALLY]

PACKAGE LEAFLET

Package leaflet: Information for the user

COVAXiS

Suspension for injection

Diphtheria, Tetanus, Pertussis (acellular, component) Vaccine
(adsorbed, reduced antigen(s) content)

Read all of this leaflet carefully before you or your child is vaccinated because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse .
- This vaccine has been prescribed for you or for your child only. Do not pass it on to others.
- If you or your child get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 What COVAXiS is and what it is used for

COVAXiS is a vaccine. Vaccines are used to protect against infectious diseases. They work by causing the body to produce its own protection against the bacteria that cause the targeted diseases.

This vaccine is used to boost protection against diphtheria, tetanus and pertussis (whooping cough) in children from the age of four years, adolescents and adults, following a complete primary course of vaccination.

Limitations in the protection provided

COVAXiS will only prevent these diseases if they are caused by the bacteria targeted by the vaccine. You or your child could still get similar diseases if they are caused by other bacteria or viruses.

COVAXiS does not contain any live bacteria or viruses and it cannot cause any of the infectious diseases against which it protects.

Remember that no vaccine can provide complete, life long protection in all people who are vaccinated.

2 What you need to know before COVAXiS is given to you or your child

To make sure that COVAXiS is suitable for you or your child, it is important to tell your doctor or nurse if

any of the points below apply to you or your child. If there is anything you do not understand, ask your doctor or nurse to explain.

Do not use COVAXiS if you or your child

- has had an allergic reaction:
  - to diphtheria, tetanus or pertussis vaccines
  - to any of the other ingredients (listed in section 6)
  - to any residual component carried over from manufacture (formaldehyde, glutaraldehyde) which may be present in trace amounts.
- has ever had a severe reaction affecting the brain within one week after a previous dose of a whooping cough vaccine
- has an acute illness with or without fever. The vaccination should be delayed until you or your child has recovered. A minor illness without fever is not usually a reason to defer vaccination. Your doctor will determine if you or your child should receive COVAXiS.

Warnings and precautions

Tell your doctor or nurse before vaccination if you or your child has

- received a booster dose of a vaccine for diphtheria and tetanus within the last 4 weeks. In this case you or your child should not receive COVAXiS and your doctor will decide on the basis of official recommendations when you or your child can receive a further injection.
- ever had a Guillain-Barré syndrome (temporary loss of movement and feeling in all or part of the body) or brachial neuritis (loss of movement, pain and numbness of the arm and the shoulder) following a previous dose of a tetanus containing vaccine. Your doctor will decide if you or your child should receive COVAXiS.
- a progressive illness affecting the brain/nerves or uncontrolled fits. Your doctor will first start treatment and vaccinate when the condition has stabilized.
- a poor or reduced immune system, due to
  - medication (e.g., steroids, chemotherapy or radiotherapy)
  - HIV infection or AIDS
  - any other illness.

  The vaccine may not protect as well as it protects people whose immune system is healthy. If possible, vaccination should be postponed until the end of such disease or treatment.
- any problems with the blood that causes easy bruising, or bleeding for a long time after minor cuts (for instance due to a blood disorder such as haemophilia or thrombocytopenia or treatment with blood thinning medicines).

Other medicines or vaccines and COVAXiS

Tell your doctor, pharmacist or nurse if you or your child is taking, has recently taken or might take any other medicines.

As COVAXiS does not contain any live bacteria, it can generally be given at the same time as other vaccines or immunoglobulins, but at a different injection site. Studies have demonstrated that COVAXiS can be used at the same time as any of the following vaccines: a hepatitis B vaccine, a poliovirus vaccine (injected or oral), an inactivated flu vaccine and a recombinant Human Papillomavirus vaccine respectively. Injections of more than one vaccine at the same time will be given in different limbs.

If you or your child is receiving medical treatment affecting you or your child's blood or immune system

(such as blood thinning medicines, steroids or chemotherapy), please refer to the section "Warnings and precautions" above.

Pregnancy, breast-feeding and fertility

Tell your doctor or nurse if you or your child is pregnant or breast-feeding, think you or your child might be pregnant or planning to have a baby. Your doctor or nurse can advise you whether or not vaccination should be delayed.

Driving and using machines

It has not been studied if the vaccine affects the ability to drive or use machines. The vaccine has no or negligible influence on the ability to drive and use machines.

3 How and when COVAXiS is given

When you or your child will be given the vaccine

Vaccination history
Your doctor will determine if COVAXiS is suitable for you or your child, depending on:

- what vaccines have been given to you or your child in the past
- how many doses of similar vaccines have been given to you or your child in the past
- when the last dose of a similar vaccine was given to you or your child

You or your child must have had the complete primary courses of diphtheria and tetanus vaccines before having COVAXiS.

It is safe to have COVAXiS if you or your child has not had the complete primary course of whooping cough vaccines but protection may not be as good as in people who have already had the whooping cough vaccine.

Your doctor will decide how long you have to wait between vaccinations.

Dosage and method of administration

Who will give you COVAXiS?

COVAXiS should be given by healthcare professionals who have been trained in the use of vaccines and at a clinic or surgery that is equipped to deal with any rare severe allergic reaction to the vaccine.

Dosage

All age groups for whom COVAXiS is indicated will receive one injection (half a millilitre).

In case you or your child experience an injury which requires preventive action for tetanus disease, your doctor may decide to give COVAXiS with or without tetanus immunoglobulin.

COVAXiS can be used for repeat vaccination. Your doctor will give you advice on repeat vaccination.

Use in children and adolescents

COVAXiS should not be used in children under 4 years of age.

Children from the age of 4 years onwards and adolescents should receive the same dosage as adults.

Method of administration

Your doctor or nurse will give you the vaccine into a muscle in the upper outer part of the arm (deltoid muscle).

Your doctor or nurse will **not** give you the vaccine into a blood vessel, into the buttocks or under the skin. In case of blood clotting disorders they may decide to inject under the skin, although this might result in more local side effects, including a small lump under the skin.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4 Possible side effects

Like all medicines, COVAXiS can cause side effects, although not everybody gets them.

Serious allergic reactions

If any of these symptoms occur after leaving the place where you or your child received the injection, you must consult a doctor IMMEDIATELY.

- difficulty in breathing
- blueness of the tongue or lips
- a rash
- swelling of the face or throat
- low blood pressure causing dizziness or collapse.

When these signs or symptoms occur they usually develop very quickly after the injection is given and while you or your child is still in the clinic or doctor's surgery. Serious allergic reactions are a very rare possibility (may affect up to 1 in 10,000 people) after receiving any vaccine.

Other side effects

The following side effects were observed during clinical studies carried out in specific age groups.

In children aged 4 to 6 years

Very common (may affect more than 1 in 10 people) :

- decreased appetite,
- headache
- diarrhoea
- tiredness
- pain
- redness and swelling in the area where the vaccine was injected.

Common (may affect up to 1 in 10 people) :

- nausea,
- vomiting,
- rash,
- aching (all over the body) or muscular weakness,
- aching or swollen joints,
- fever,
- chills,
- underarm lymph node disorder.

In adolescents aged 11 to 17 years

Very common (may affect more than 1 in 10 people) :

- headache
- diarrhoea
- nausea
- aching (all over the body) or muscular weakness
- aching or swollen joints
- tiredness/weakness
- feeling unwell
- chills
- pain
- redness and swelling in the area where the vaccine was injected.

Common (may affect up to 1 in 10 people) :

- vomiting,
- rash
- fever
- underarm lymph node disorder.

In adults aged 18 to 64 years

Very common (may affect more than 1 in 10 people) :

- headache
- diarrhoea
- aching (all over the body) or muscular weakness
- tiredness/weakness
- feeling unwell
- pain redness and swelling in the area where the vaccine was injected.

Common (may affect up to 1 in 10 people) :

- nausea,
- vomiting
- rash
- aching or swollen joints
- fever
- chills
- underarm lymph node disorder.

The following additional adverse events have been reported in the various recommended age groups during the commercial use of COVAXiS. The frequency of these adverse events cannot be precisely calculated, as it would be based on voluntary reporting in relation to the estimated number of vaccinated persons.

- Allergic / serious allergic reactions (how you can recognize such a reaction, you can find in the beginning of section 4), 'pins and needles' or numbness, paralysis of part or all the body (Guillain-Barré syndrome), inflammation of the nerves in the arm (brachial neuritis), loss of function in the nerve that supplies the facial muscles (facial palsy), fits (convulsions), fainting, inflammation of the spinal cord (myelitis), inflammation of the muscular part of the heart (myocarditis), itching, hives, inflammation of a muscle (myositis), extensive limb swelling associated with redness, warmth, tenderness or pain in the area where the vaccine was injected, bruising or abscess in the area where the vaccine was injected.

Reporting of side effects

If you or your child get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5 How to store COVAXiS

Keep this medicine out of the sight and reach of children.

COVAXiS must not be used after the expiry date which is stated on the label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Discard the vaccine if it has been frozen.

Keep the container in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6 Contents of the pack and other information

What COVAXiS contains

The active substances in each dose (0.5 mL) of vaccine are:

Diphtheria Toxoid	not less than 2 International Units (2 Lf)
Tetanus Toxoid	not less than 20 International Units (5 Lf)
Pertussis Antigens:	
Pertussis Toxoid	2.5 micrograms
Filamentous Haemagglutinin	5 micrograms
Pertactin	3 micrograms
Fimbriae Types 2 and 3	5 micrograms
Adsorbed on Aluminium Phosphate	1.5 mg (0.33 mg Aluminium)

The other ingredients are: phenoxyethanol, water for injections

What COVAXiS looks like and contents of the pack

COVAXiS is presented as a suspension for injection in a vial (0.5 mL): pack size of 1 or 10.

Not all pack sizes may be marketed.

The normal appearance of the vaccine is a cloudy white suspension, which may sediment during storage. After shaking well it is a uniformly white liquid.

Marketing Authorisation Holder and Manufacturer

[TO BE COMPLETED NATIONALLY]

The manufacturer responsible for batch release is:

[TO BE CHOSEN AS APPROPRIATE]
[For all countries:]
Sanofi Pasteur SA
2, avenue Pont Pasteur
69007 Lyon
France

[For countries in which sanofi pasteur is MAH:]
Sanofi-Aventis Zrt., Budapest
Logistics and Distribution Platform
H-1225 Budapest
Building DC5, Campona utca. 1
(Harbor Park)
Hungary

This medicinal product is authorised in the Member States of the EEA under the following names:

Germany:	Covaxis
Austria, Belgium, Denmark, Finland, France, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden:	Triaxis
Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia, Slovenia, United Kingdom:	Adacel

This leaflet was last revised in {**month YYYY**}.

The following information is intended for healthcare professionals only:

Instructions for use

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

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. If these conditions exist, the product should not be administered.

When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place.

Needles should not be recapped.