

1 NAME OF THE MEDICINAL PRODUCT

ADACEL 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	2 Lf
Tetanus Toxoid	5 Lf
Pertussis Toxoid	2.5 micrograms
Filamentous Haemagglutinin	5 micrograms
Pertactin	3 micrograms
Fimbriae Types 2 and 3	5 micrograms
Aluminium (aluminium phosphate by calculation)	0.33±0.003mg (1.5mg)

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

ADACEL appears as a cloudy white suspension.

CLINICAL PARTICULARS

4.1. Therapeutic indications

ADACEL is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis in children, adolescents and adults aged 4 to 64 years.

ADACEL is not to be used for the treatment of disease caused by *B.ordetella pertussis*, *C.-orynebacterium diphtheriae* or *Clostridium tetani* infections.

4.2. Posology and method of administration

Posology

Recommended Dose

The immunization schedule with ADACEL should follow local recommendations. ADACEL (0.5mL) should be administered as a booster dose by the intramuscular route.

Re-dosing with ADACEL can be used to boost immunity to diphtheria, tetanus and pertussis at 5 to 10 year intervals.

The preferred site is into the deltoid muscle.

Fractional doses (doses <0.5 mL) should not be given. The effect of fractional doses on the safety and efficacy has not been determined.

The use of ADACEL in management of tetanus-prone wounds should follow local recommendations. Canada's National Advisory Committee on Immunization (NACI) and US Advisory Committee on Immunization Practices (ACIP) have issued guidelines for tetanus prophylaxis in routine wound management as shown in the Table below

NACI Recommended Use of Immunizing Agents in Wound Management

History of Tetanus Immunization	Clean, Minor Wounds		All Other Wounds	
	Td *	TIG † (Human)	Td *	TIG † (Human)
Uncertain or <3 doses of an immunization series ‡	Yes	No	Yes	Yes
≥ 3 doses received in an immunization series ‡	No §	No	No **	No ††

* Adult-type tetanus and diphtheria toxoid.

† Tetanus immune globulin, given at a separate site from the Td.

‡ Primary immunization is at least 3 doses at age appropriate intervals.

§ Yes, if >10 years since last booster.

** Yes, if >5 years since last booster.

†† Yes, if persons are known to have a significant humoral immune deficiency state (e.g., hiv, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Persons who have completed primary immunization against tetanus and who sustain wounds that are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (e.g., wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years.

Method of administration

Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.

Shake the vial well until a uniform, cloudy, suspension results. Cleanse the vial stopper with a suitable germicide prior to withdrawing the dose. Do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient, to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines.

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. Administer the total volume of 0.5 mL intramuscularly (IM). The preferred site of injection is the deltoid muscle.

4.3 Contraindications

- ADACEL 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.
- ADACEL 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, administration of ADACEL 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

ADACEL should not be used for primary immunization.

Regarding the interval between a booster dose of ADACEL 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 ADACEL 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 occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid, including ADACEL should be based on careful consideration of the potential benefits and possible risks.

ADACEL 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 ADACEL by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

Syncope (fainting) can occur following, or even before, administration of injectable vaccines, including ADACEL. Procedures should be in place to prevent falling injury and manage syncopal reactions.

Other considerations

As with any vaccine, vaccination with ADACEL 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.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interaction

Based on the results of concomitant use clinical studies, ADACEL can be administered concomitantly with inactivated Influenza vaccine, Hepatitis B vaccine and Inactivated or Oral Poliomyelitis vaccine. Additionally, ADACEL can be administered with human papilloma virus vaccine (HPV) and/or Meningococcal Polysaccharide (Serogroups A, C, Y, and W) (MenACYW) conjugate vaccines (either all three vaccines concomitantly or in pairs) (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 ADACEL 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

Safety data from 4 randomized controlled trials (310 pregnancy outcomes), 2 prospective observational studies (2670 pregnancy outcomes), 4 retrospective observational studies (81,701 pregnancy outcomes), and from passive surveillance of women who received ADACEL or ADACEL POLIO (Tdap-IPV; containing the Tdap component of ADACEL) during the 2nd or 3rd trimester have shown no vaccine-related adverse effect on pregnancy or on the health of the fetus/newborn child. As with other inactivated vaccines, it is not expected that vaccination with ADACEL during any trimester would harm the fetus. The benefits versus the risks of administering ADACEL during pregnancy should be evaluated.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development.

Limited clinical data have shown there is interference with the immune response to other antigens (i.e. diphtheria, tetanus, polio, pneumococcal, meningococcal) in infants born to women vaccinated with ADACEL during pregnancy. However, in most of the cases, the antibody concentrations remain above the thresholds established as protective. The clinical relevance of this observation is unknown.

Breast-feeding

It is not known whether the active substances included in ADACEL are excreted in human milk but antibodies to the vaccine antigens have been found to be transferred to the suckling offspring of rabbits. Two animal developmental studies conducted in rabbits have 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 ADACEL to their mothers has not been studied. As ADACEL is inactivated, any risk to the infant is unlikely. The risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.

Fertility

ADACEL 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. ADACEL 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 ADACEL 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.

The safety analysis of concomitant use of either ADACEL or ADACEL POLIO administered with MenACYW (Menactra or MenQuadfi) and/or HPV (Gardasil or Gardasil 9) vaccines included 5,122 healthy male and female subjects aged 10 to 17 years from 6 clinical trials.

The overall safety profile of ADACEL or ADACEL POLIO was similar when all three vaccines were administered concomitantly compared to coadministered pairs (ADACEL and Menactra or ADACEL/ADACEL POLIO and Gardasil/Gardasil 9). The safety profile of coadministered ADACEL POLIO and Gardasil/Gardasil 9 was similar to Gardasil/Gardasil 9 administered alone.

In clinical studies, injection site reactions (pain, erythema, swelling, and bruising), as well as headache, malaise, and myalgia were observed more frequently when all three vaccines were administered together or in pairs, compared to when they were administered alone. Overall, the differences observed in injection site reactions were < 10%, while the differences in headache, malaise, and myalgia ranged from < 10% to < 28%. The difference in fever rates across clinical studies was < 2%.

The majority of 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 ADACEL 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
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		Arthralgia or Joint swelling

System Organ Class	Frequency	Children (4 to 6 Years)	Adolescents (11 to 17 Years)	Adults (18 to 64 Years)
		weakness, 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*, Injection site nodule*		

* 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 ADACEL 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 ADACEL 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.

Any suspected adverse events should be reported to the Ministry of Health (www.health.gov.il) according to the National Regulation by using an online form <https://sideeffects.health.gov.il>

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 ADACEL 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 ADACEL

Antibody	Criteria	Children (4 - 6 years) ¹ (N=265) %	Adolescents (11 - 17 years) ² (N=527) %	Adults (18 - 64 years) ² (N=743) %
Diphtheria (SN, IU/mL)	≥0.1	100	99.8	94.1
Tetanus (ELISA, IU/mL or EU/mL)	≥0.1	100	100	100
Pertussis (ELISA, EU/mL)	Booster Response ³			
PT		91.9	92.0	84.4
FHA		88.1	85.6	82.7
PRN		94.6	94.5	93.8
FIM		94.3	94.9	85.9

DTaP: diphtheria toxoid [paediatric dose], tetanus and acellular pertussis; ELISA: Enzyme Linked Immunoassay; EU: ELISA units; IU: international units; N: number of participants with available data; SN: seroneutralisation.

¹ Study Td508 was conducted in Canada with children 4-6 years of age.

² Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age.

³ For children in Study Td508 who were previously primed with DTaP 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 in Study Td506, 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 ADACEL 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 acellular pertussis infant DTaP formulation confirmed a protective efficacy of 85% against pertussis disease, it is considered that ADACEL had elicited protective immune responses. The pertussis antibody levels for all antigens following a booster dose of ADACEL 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 ADACEL 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 (PPI Population¹)

	Adolescents (11-17 years) ²	Adults (18-64 years) ²
	ADACEL/DTaP ³ GMC Ratio (95% CIs) ⁴	ADACEL/DTaP ³ GMC Ratio (95% CIs) ⁴
Participants	N=524-526	N=741
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)

DTaP: diphtheria toxoid [paediatric dose], tetanus and acellular pertussis; GMC: Geometric Mean Concentration; N: number of participants with available data; PPI: per protocol immunogenicity

¹ Eligible participants for whom immunogenicity data were available.

² Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age. Antibody GMCs, measured in ELISA units were calculated separately for infants, adolescents and adults.

³ 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 study Td506).

⁴ GMCs following ADACEL were non-inferior to GMCs following DTaP (lower limit of 95% CI on the ratio of GMCs for ADACEL divided by DTaP >0.67).

Antibody persistence

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

Table 4: Persistence of Seroprotection/Seropositivity Rates (%) in Children, Adolescents and Adults at 3-, 5- and 10- years following a dose of ADACEL (PPI Population¹)

		Children (4-6 years) ²	Adolescents (11-17 years) ³		Adults (18-64 years) ³			
Time since ADACEL dose		5 years	3 years	5 years	10 years	3 years	5 years	10 years
Participants		N=128-150	N=300	N=204-206	N=28-39	N=292	N=237-238	N=120-136
Antibody		% Seroprotection/Seropositivity						
Diphtheria (SN, IU/mL)	≥ 0.1	86.0	97.0	95.1	94.9	81.2	81.1	84.6
	≥ 0.01	100	100	100	100	95.2	93.7	99.3
Tetanus (ELISA, IU/mL)	≥ 0.1	97.3	100	100	100	99.0	97.1	100
Pertussis (ELISA, EU/mL)	Sero- positivity ⁴							
PT		63.3	97.3	85.4	82.1	94.2	89.1	85.8
FHA		97.3	100	99.5	100	99.3	100	100
PRN		95.3	99.7	98.5	100	98.6	97.1	99.3
FIM		98.7	98.3	99.5	100	93.5	99.6	98.5

ELISA: Enzyme Linked Immunoassay; EU: ELISA units; IU: international units; N: number of participants with available data; PPI: per protocol immunogenicity; SN: seroneutralisation;

¹ Eligible participants for whom immunogenicity data were available for at least one antibody at the specified time-point.

² Study Td508 was conducted in Canada with children 4-6 years of age.

³ Study Td506 was conducted in the United States with adolescents 11-17 years of age and adults 18-64 years of age.

⁴ Percentage of participants with antibodies ≥ 5 EU/mL for PT, ≥ 3 EU/mL for FHA and PRN, and ≥ 17 EU/mL for FIM for the 3 year follow-up; ≥ 4 EU/mL for PT, PRN and FIM, and ≥ 3 EU/mL for FHA for the 5-year and 10-year follow-up.

Immunogenicity in persons not previously vaccinated or with an unknown vaccination status

After administration of one dose of ADACEL POLIO (Tdap-IPV; containing the same amounts of tetanus, diphtheria and pertussis antigens as ADACEL) to 330 adults ≥40 years of age that had not received any diphtheria- and tetanus-containing vaccine in the past 20 years:

- ≥95.8% of adults were seropositive (≥ 5 EU/mL) for antibodies to all vaccine-containing pertussis antigens,
- 82.4% and 92.7% were seroprotected against diphtheria at a threshold ≥0.1 and ≥0.01 IU/mL, respectively,
- 98.5% and 99.7% were seroprotected against tetanus at a threshold ≥0.1 and ≥0.01 IU/mL, respectively,
- and ≥98.8% were seroprotected against polio (types 1, 2 and 3) at a threshold ≥1:8 dilution.

After administration of two additional doses of diphtheria- tetanus- and polio-containing vaccine to 316 subjects, one and six months after the first dose, the seroprotection rates against diphtheria were 94.6% and 100% (≥ 0.1 and ≥ 0.01 IU/mL, respectively), against tetanus 100% (≥ 0.1 IU/mL), and against polio (types 1, 2 and 3) 100% ($\geq 1:8$ dilution).

Immunogenicity following repeat vaccination

The immunogenicity of ADACEL following repeat vaccination 10 years after a previous dose of ADACEL or ADACEL POLIO, has been evaluated. One month post-vaccination $\geq 98.5\%$ of study participants achieved seroprotective antibody levels (≥ 0.1 IU/ml) for diphtheria and tetanus, and $\geq 84\%$ 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 $< \text{LLOQ}$; ≥ 4 times the pre-vaccination level if that was $\geq \text{LLOQ}$ 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, ADACEL 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

2 Phenoxyethanol
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials

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, 5, 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.

8. MARKETING AUTHORISATION HOLDER:

Sanofi Israel Ltd., Greenwork Complex, P.O box 47, Yakum

9. MARKETING AUTHORISATION NUMBER

142-16-32020-00

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