SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

ABRYSVO, 120 µg powder and solvent for solution for injection

[Respiratory syncytial virus vaccine (bivalent, recombinant)]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0,5 mL) contains:

RSV subgroup A stabilised prefusion F antigen[1,2] 60 micrograms

RSV subgroup B stabilised prefusion F antigen[1,2] 60 micrograms

(RSV antigens)

[1]glycoprotein F stabilised in the prefusion conformation

[2]produced in Chinese Hamster Ovary cells by recombinant DNA technology.

Excipient with known effects

Each vial contains 11,3 mg sucrose and 22,5 mg mannitol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

The powder is white.

The solvent is a clear, colourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ABRYSVO is indicated for

- Passive protection against lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age following maternal immunisation during pregnancy. See sections 4.2 and 5.1.
- Active immunisation of individuals 60 years of age and older for the prevention of lower respiratory tract disease caused by RSV.

The use of ABRYSVO should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Pregnant individuals

A single dose of 0,5 mL should be administered between weeks 28 and 36 of gestation (see sections 4.4 and 5.1).

Individuals 60 years of age and older
A single dose of 0,5 mL should be administered.

Paediatric population
The safety and efficacy of ABRYSVO in children (from birth to less than 18 years of age) have not yet been established. Limited data are available in pregnant adolescents and their infants (see section 5.1).

Method of administration

ABRYSVO is for intramuscular injection into the deltoid region of the upper arm.

ABRYSVO should not be mixed with any other vaccines or medicines.

For instructions on reconstitution and handling of the medicine before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to RSV antigens or to any of the excipients of ABRYSVO listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicines, the name and the batch number of the administered medicine should be clearly recorded.

Hypersensitivity and anaphylaxis

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the ABRYSVO.

Anxiety-related reactions

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. It is important that procedures are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from an acute febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Thrombocytopenia and coagulation disorders

ABRYSVO should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding or bruising may occur following an intramuscular administration to these individuals.

Immunocompromised individuals

The efficacy and safety of the vaccine have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of ABRYSVO may be lower in immunosuppressed individuals.

Individuals less than 24 weeks of gestation

ABRYSVO has not been studied in pregnant individuals less than 24 weeks of gestation. Since protection of the infant against RSV depends on transfer of maternal antibodies across the placenta, ABRYSVO should be administered between weeks 28 and 36 of gestation (see sections 4.2 and 5.1).

Limitations of vaccine effectiveness

As with any vaccine, a protective immune response may not be elicited after vaccination.

Excipients

Sodium content

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

4.5 Interaction with other medices and other forms of interaction

ABRYSVO can be administered concomitantly with seasonal influenza vaccine (QIV, surface antigen, inactivated, adjuvanted*).* In a randomised study in adults 65 years of age and older, the criteria for non-inferiority of the immune responses in the co-administration versus the separate administration group were met. However, numerically lower RSV A and B neutralising titres and numerically lower influenza A and B haemagglutination inhibition titres were observed when ABRYSVO and inactivated adjuvanted seasonal influenza vaccine were co-administered than when they were administered separately. The clinical relevance of this finding is unknown.

A minimum interval of two weeks is recommended between administration of ABRYSVO and administration of a tetanus, diphtheria and acellular pertussis vaccine (Tdap). There were no safety concerns when ABRYSVO co-administered with Tdap in healthy non-pregnant women. Immune responses to RSV A, RSV B, diphtheria and tetanus on co-administration were non-inferior to those after separate administration. However, the immune responses to the pertussis components were lower on co-administration compared to separate administration and did not meet the criteria for non-inferiority. The clinical relevance of this finding is unknown.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on pregnant women (more than 4 000 exposed outcomes) indicate no malformative nor feto/neonatal toxicity.

Results from animal studies with ABRYSVO do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

In a phase 3 study (Study 1), maternal adverse events reported within 1 month after vaccination were similar in the ABRYSVO group (14 %) and the placebo group (13 %).

No safety signals were detected in infants up to 24 months of age. The incidences of adverse events reported within 1 month after birth in infants were similar in the ABRYSVO group (37 %) and the placebo group (35 %). Major birth outcomes assessed in the ABRYSVO group compared to placebo included premature birth (201 (6 %) and 169 (5 %), respectively), low birth weight (181 (5 %) and 155 (4 %), respectively) and congenital anomalies (174 (5 %) and 203 (6 %), respectively).

Breastfeeding

It is unknown whether ABRYSVO are excreted in human milk. No adverse effects of ABRYSVO have been shown in breastfed newborns of vaccinated mothers.

Fertility

No human data on the effect of ABRYSVO on fertility are available.

Animal studies do not indicate direct or indirect harmful effects with respect to female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

ABRYSVO has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Pregnant individuals
In pregnant women at 24 - 36 weeks of gestation the most frequently reported adverse reactions were vaccination site pain (41 %), headache (31 %) and myalgia (27 %). The majority of local and systemic reactions in maternal participants were mild to moderate in severity and resolved within 2 - 3 days of onset.

Individuals 60 years of age and older

In individuals 60 years of age and older the most frequently reported adverse reaction was vaccination site pain (11 %). The majority of reactions were mild to moderate in severity and resolved within 1 - 2 days of onset.

Tabulated list of adverse reactions

The safety of administering a single dose of ABRYSVO to pregnant women at 24 - 36 weeks of gestation (n=3 682) and to individuals 60 years of age and older (n=18 575) was evaluated in phase 3 clinical trials.

Adverse reactions are listed below by MedDRA body system organ class and the following frequency 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). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 1. Adverse reactions following administration of ABRYSVO in pregnant individuals ≤ 49 years

MedDRA system organ class	**Frequency**	**Adverse reaction**
Nervous system disorders	Very common	Headache

Musculoskeletal and connective tissue disorders	Very common	Myalgia
General disorders and administration site conditions	Very common	Vaccination site pain
	Common	Vaccination site redness
	Common	Vaccination site redness

Table 2. Adverse reactions following administration of ABRYSVO in individuals ≥ 60 years

MedDRA system organ class	**Frequency**	**Adverse reaction**
Immune system disorders	Very rare	Hypersensitivity
Nervous system disorders	Rare[a]	Guillain-Barré syndrome
General disorders and administration site conditions	Very common	Vaccination site pain
	Common	Vaccination site redness
	Common	Vaccination site redness

In a study in individuals 60 years of age and older, one case of Guillain-Barré syndrome and one case of Miller Fisher syndrome were reported with onset of 7 and 8 days, respectively, after receiving ABRYSVO and assessed by the investigator as possibly related to the administered vaccine. Both cases had either confounding factors or an alternative aetiology. One additional case, with onset 8 months after receiving ABRYSVO, was assessed as not related to the administered vaccine by the investigator. One case of Guillain-Barré syndrome was reported in the placebo group 14 months after administration.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit / risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Report any suspected adverse drug reactions associated with the use of the medicine directly to Pfizer via ZAF.AEReporting@pfizer.com.

4.9 Overdose

Overdose with ABRYSVO, is unlikely due to its single dose presentation.

There is no specific treatment for an overdose with ABRYSVO. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, other viral vaccines; ATC code: J07BX05

Mechanism of action

Respiratory syncytial virus vaccine contains two recombinant stabilised RSV prefusion F antigens representing subgroups RSV A and RSV B. Prefusion F is the primary target of neutralising antibodies that block RSV infection. Following intramuscular administration, the prefusion F antigens elicit an immune response, which protects against RSV associated lower respiratory tract disease.

In infants born to mothers who were vaccinated with Respiratory syncytial virus vaccine between weeks 24 and 36 of gestation, protection against RSV-associated lower respiratory tract disease is due to transplacental transfer of RSV neutralising antibodies. Adults 60 years of age and older are protected by active immunisation.

Clinical efficacy

Infants from birth through 6 months of age by active immunisation of pregnant individuals

Study 1 is a phase 3, multicentre, randomised (1:1), double-blind, placebo-controlled study to assess the efficacy of a single dose of Respiratory syncytial virus vaccine in the prevention of RSV associated lower respiratory tract disease in infants born to pregnant individuals vaccinated between weeks 24 and 36 of gestation. The need for revaccination with subsequent pregnancies has not been established.

RSV-associated lower respiratory tract illness was defined as a medically attended visit with a reverse transcription-polymerase chain reaction (RT-PCR) confirmed RSV illness with one or more of the following respiratory symptoms: fast breathing, low oxygen saturation (SpO2 < 95 %) and chest wall indrawing. RSV-associated severe lower respiratory tract illness was defined as an illness that met the lower respiratory tract illness RSV criteria plus at least one of the following: very fast breathing, low oxygen saturation (SpO2 < 93 %), high-flow oxygen supplementation via nasal cannula or mechanical ventilation, ICU admission for >4 hours and/or failure to respond/unconscious.

In this study, 3 695 pregnant individuals with uncomplicated, singleton pregnancies were randomised to the Respiratory syncytial virus vaccine group and 3 697 to placebo.

Vaccine efficacy (VE) was defined as the relative risk reduction of the endpoint in the Respiratory syncytial virus vaccine group compared to the placebo group for infants born to pregnant individuals who received the assigned intervention. There were two primary efficacy endpoints, assessed in parallel, severe RSV positive medically attended lower respiratory tract illness and RSV positive medically attended lower respiratory tract illness, occurring within 90, 120, 150 or 180 days after birth.

Of the pregnant women who received Respiratory syncytial virus vaccine, 65 % were White, 20 % were Black or African American and 29 % were Hispanic/Latino. The median age was 29 years (range 16 - 45 years); 0,2 % of participants were under 18 years of age and 4,3 % were under 20 years of age. The median gestational age at vaccination was 31 weeks and 2 days (range 24 weeks and 0 days to 36 weeks and 4 days). The median infant gestational age at birth was 39 weeks and 1 day (range 27 weeks and 3 days to 43 weeks and 6 days).

Vaccine efficacy is presented in Tables 3 and 4.

Table 3 - Vaccine efficacy of Respiratory syncytial virus vaccine against severe medically attended lower respiratory tract illness caused by RSV in infants from birth through 6 months of age by active immunisation of pregnant individuals – Study 1

Time period	Respiratory syncytial virus vaccine Number of cases N=3 495	Placebo Number of cases N=3 480	VE % (CI)[a]
90 days	6	33	81,8 (40,6; 96,3)
120 days	12	46	73,9 (45,6; 88,8)
150 days	16	55	70,9 (44,5; 85,9)
180 days	19	62	69,4 (44,3; 84,1)
CI = confidence interval; VE = vaccine efficacy [a]99,5 % CI at 90 days; 97,58 % CI at later intervals			

Table 4 - Vaccine efficacy of Respiratory syncytial virus vaccine against medically attended lower respiratory tract illness caused by RSV in infants from birth through 6 months of age by active immunisation of pregnant individuals - Study 1

Time period	Respiratory syncytial virus vaccine Number of cases N=3 495	Placebo Number of cases N=3 480	VE % (CI)[a]
90 days	24	56	57,1 (14,7; 79,8)
120 days	35	81	56,8 (31,2; 73,5)
150 days	47	99	52,5 (28,7; 68,9)
180 days	57	117	51,3 (29,4; 66,8)
CI = confidence interval; VE = vaccine efficacy [a]99,5 % CI at 90 days; 97,58 % CI at later intervals			

A post-hoc analysis of VE by maternal gestational age was conducted. For severe medically attended lower respiratory tract illness occurring within 180 days, VE was 57,2 % (95 % CI 10,4; 80,9) for women vaccinated early in pregnancy (24 to < 30 weeks) and 78,1 % (95 % CI 52,1; 91,2) for women vaccinated later in the pregnancy eligible window (30 to 36 weeks). For medically attended lower respiratory tract illness occurring within 180 days, VE was 30,9 % (95 % CI -14,4; 58,9) for women vaccinated early in pregnancy (24 to < 30 weeks) and 62,4 % (95 % CI 41,6; 76,4) for women vaccinated later in the pregnancy eligible window (30 to 36 weeks).

Active immunisation of individuals 60 years of age and older

Study 2 is a phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the efficacy of Respiratory syncytial virus vaccine in the prevention of RSV-associated lower respiratory tract illness in individuals 60 years of age and older.

RSV-associated lower respiratory tract illness was defined as RT-PCR confirmed RSV illness with two or more or three or more of the following respiratory symptoms within 7 days of symptom onset and lasting more than 1 day during the same illness: new or increased cough, wheezing, sputum production, shortness of breath or tachypnoea (≥ 25 breaths/min or 15 % increase from resting baseline).

Participants were randomised (1:1) to receive Respiratory syncytial virus vaccine (n=18 488) or placebo (n=18 479). Enrolment was stratified by age 60 - 69 years (63 %), 70 - 79 years (32 %) and ≥ 80 years (5 %). Subjects with stable chronic underlying conditions were eligible for this study and 52 % of participants had at least 1 prespecified condition; 16 % of participants were enrolled with stable chronic cardiopulmonary conditions such as asthma (9 %), chronic obstructive pulmonary disease (7 %) or congestive heart failure (2 %). Immunocompromised individuals were ineligible.

The primary objective was assessment of vaccine efficacy (VE), defined as the relative risk reduction of first episode of RSV-associated lower respiratory tract illness in the Respiratory syncytial virus vaccine group compared to the placebo group in the first RSV season.

Of the participants who received Respiratory syncytial virus vaccine, 51 % were male and 80 % were White, 12 % were Black or African American and 41 % were Hispanic/Latino. The median age of participants was 67 years (range 59 - 95 years).

At the end of the first RSV season the analysis demonstrated statistically significant efficacy for Respiratory syncytial virus vaccine for reduction of RSV-associated lower respiratory tract illness with ≥2 symptoms and with ≥3 symptoms.

Table 4 Vaccine efficacy of Respiratory syncytial virus vaccine against RSV disease - active immunisation of individuals 60 years of age and older – Study 2

Efficacy endpoint	Respiratory syncytial virus vaccine Number of cases N=18 058	Placebo Number of cases N=18 076	VE (%) (95 % CI)
First episode of RSV-associated lower respiratory tract illness with ≥2 symptoms[a]	15	43	65,1 (35,9; 82,0)
First episode of RSV-associated lower respiratory tract illness with ≥3 symptoms[b]	2	18	88,9 (53,6; 98,7)

CI – confidence interval; RSV – respiratory syncytial virus; VE – vaccine efficacy

[a] In an exploratory analysis in RSV subgroup A (Respiratory syncytial virus vaccine n=3, placebo n=16 VE was 81,3 % (CI 34,5; 96,5); and in RSV subgroup B (Respiratory syncytial virus vaccine n=12, placebo n=26) VE was 53,8 % (CI 5,2; 78,8).

[b] In an exploratory analysis in RSV subgroup A (Respiratory syncytial virus vaccine n=1, placebo n=5) VE was 80,0 % (CI -78,7; 99,6); and in RSV subgroup B (Respiratory syncytial virus vaccine n=1, placebo n=12) VE was 91,7 % (CI 43,7; 99,8).

Paediatric population

Refer to Section 4.2.

5.2 Pharmacokinetic properties

Not applicable.

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 and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Trometamol

Trometamol hydrochloride

Sucrose

Mannitol

Polysorbate 80

Sodium chloride

Hydrochloric acid (for pH adjustment)

Solvent

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

3 years

The unopened vial is stable for 5 days when stored at temperatures from 8 °C to 30 °C. At the end of this period ABRYSVO should be used or discarded. This information is used to guide healthcare professionals in case of temporary temperature excursions only.

After reconstitution

ABRYSVO should be administered immediately after reconstitution or within 4 hours if stored between 15 °C and 30 °C. Do not freeze.

Chemical and physical in-use stability has been demonstrated for 4 hours between 15 °C and 30 °C. From a microbiological point of view, the medicine should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store in a refrigerator (2 °C to 8 °C).

Do not freeze.

Discard if the carton has been frozen.

For storage conditions after reconstitution of the medicine, see section 6.3.

6.5 Nature and contents of container

Powder

Powder for 1 dose in a 2 ml vial (clear, colourless, type 1, glass or equivalent) with a stopper (synthetic chlorobutyl rubber) and a flip off cap (polypropylene)

Solvent

Solvent for 1 dose in a 1 ml pre-filled syringe (type 1 glass) with a stopper (synthetic chlorobutyl rubber) and a tip cap (synthetic isoprene/bromobutyl blend rubber)

Vial adaptor

Sterile vial adaptor

Pack size

Pack containing 1 vial of powder, 1 pre-filled syringe of solvent, 1 vial adaptor with 1 needle or without needles.

Pack containing 5 vials of powder, 5 pre-filled syringes of solvent, 5 vial adaptors with 5 needles or without needles.

Pack containing 10 vials of powder, 10 pre-filled syringes of solvent, 10 vial adaptors with 10 needles or without needles.

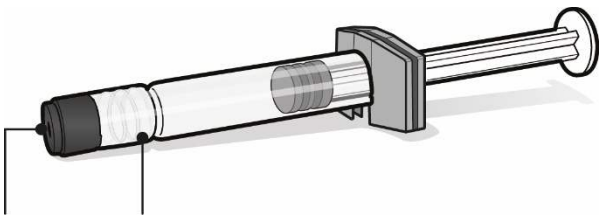
Not all pack sizes may be marketed.

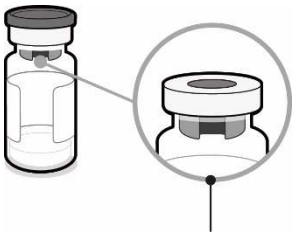
6.6 Special precautions for disposal and other handling

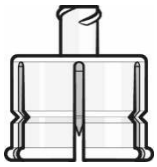
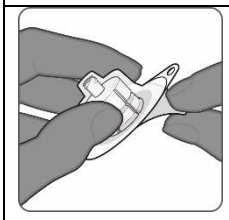
ABRYSVO must be reconstituted prior to the administration by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder using the vial adaptor.

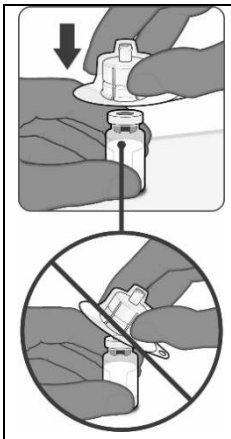
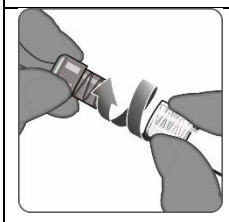
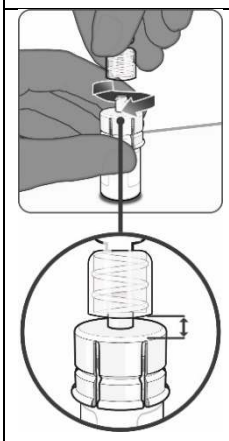
The vaccine must be reconstituted only with the solvent provided.

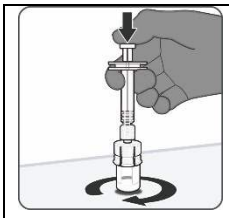
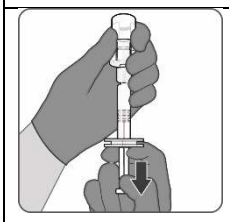
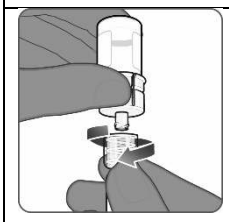
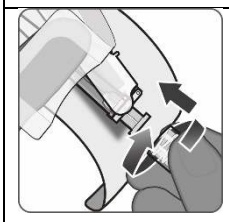
Preparation for administration

<table>
<tr><td colspan="2">Pre-filled syringe containing solvent for ABRYSVO
 
Syringe cap Luer lock adaptor

Vial containing antigens for ABRYSVO (powder)
 
Vial stopper (with flip off cap removed)

Vial adaptor
  </td></tr>
<tr><td colspan="2"></td></tr>
<tr><td>  </td><td>Step 1. Prepare vial adaptor
• Remove plastic flip off cap from vial and wipe the rubber stopper.
• Open the packaging containing the vial adaptor by peeling the top cover off.
• Do not remove the vial adaptor from its package.</td></tr>
</table>

	**Step 2. Attach the vial adaptor to the vial containing antigens for ABRYSVO** • Hold the base of the vial on a flat surface. • Keep the vial adaptor in the packaging and orient it vertically over the centre of the vial so that the adaptor spike aligns with the centre of the vial's rubber stopper. • Connect the vial adaptor to the vial with a straight downward push. The vial adaptor will lock into place. • Do not push vial adaptor in at an angle as this may result in leaking during use. • Remove the vial adaptor packaging.
	**Step 3. Remove syringe cap** • For all syringe assembly steps, hold the syringe only by the Luer lock adaptor located at the tip of the syringe. This will prevent the Luer lock adaptor from detaching during use. • Remove the syringe cap by slowly turning the cap anti-clockwise while holding the Luer lock adaptor.
	**Step 4. Connect syringe to the vial adaptor** • Hold the syringe's Luer lock adaptor and connect it to the vial adaptor by turning clockwise. • Stop turning when you feel resistance, overtightening the syringe may result in leaking during use. • Once the syringe is securely attached to the vial adaptor, there will be a small space between the top of the vial adaptor and the Luer lock adaptor of the syringe.

	**Step 5. Inject solvent and gently swirl** • Inject the entire contents of the syringe containing the solvent into the vial. • Do not remove the empty syringe. • While holding the plunger rod down, gently swirl the vial in a circular motion until the powder is completely dissolved (approximately 1 - 2 minutes). • Do not shake.
	**Step 6. Withdraw the contents** • Invert the vial completely with the vial adaptor and syringe still attached. • Slowly withdraw the entire contents into the syringe. • Drawing up all obtainable content ensures a complete 0,5 mL dose for administration. • Do not pull the plunger rod out.
	**Step 7. Disconnect syringe** Hold the Luer lock adaptor of the syringe and disconnect the syringe from the vial adaptor by turning anti-clockwise.
	**Step 8. Attach needle** • Attach a sterile needle suitable for intramuscular injection to the pre-filled syringe by turning clockwise. • Do not overtighten the needle as this may result in leaking during use.
Step 9. Visual inspection • The prepared vaccine is a clear and colourless solution. • Visually inspect the vaccine for large particulate matter and discolouration prior to administration. Do not use if large particulate matter or discolouration is found.	

Disposal

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pfizer Laboratories (Pty) Ltd

Building 2, 1st Floor,

Maxwell Office Park, Magwa Crescent, Waterfall City,

Midrand, Gauteng, 1685

South Africa

Tel: +27(0)11 320 6000 / 0860 734 937 (Toll-free South Africa)

8. REGISTRATION NUMBERS

59/24.4/0374

9. DATE OF FIRST AUTHORISATION

10 December 2024

10. DATE OF REVISION OF THE TEXT