

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

EFLUELDA

suspension for injection in pre-filled syringe

Trivalent influenza vaccine (inactivated, split-virion), 60 micrograms HA/strain

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus (inactivated, split) of the following strains*:

A/Victoria/4897/2022 (H1N1)pdm09-like strain60 micrograms HA**

A/Croatia/10136RV/2023 (H3N2)-like strain.....60 micrograms HA**

B/Austria/1359417/2021 (B/Victoria lineage)-like strain60 micrograms HA**

For one dose of 0.5 ml.

* propagated in embryonated chicken eggs

** haemagglutinin

This vaccine complies with the WHO recommendations (in the Northern Hemisphere) for the 2025/2026 season.

EFLUELDA may contain traces of egg, such as ovalbumin, and traces of formaldehyde, used during the manufacturing process (see section 4.3).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringes.

EFLUELDA, after being gently agitated, is an opalescent, colourless liquid.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

EFLUELDA is indicated for the active immunization of adults 60 years and older for the prevention of influenza disease.

The use of EFLUELDA should be based in accordance with official recommendations on vaccination against influenza.

4.2. Posology and method of administration

Posology

In patients aged 60 years and over: one 0.5 ml dose.

Paediatric population

The safety and efficacy of EFLUELDA in children under 18 years of age have not been established.

Method of administration

This vaccine is preferably administered via the intramuscular route. However, the subcutaneous route can also be used.

The intramuscular injection is preferably in the deltoid region. This vaccine should not be injected into

the buttocks or into areas that may be the site of a major nervous trunk.

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

4.3. Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1, or to any of the ingredients that may be present in traces, such as eggs (ovalbumin, chicken protein) and formaldehyde.

4.4. Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name of the administered product should be clearly recorded. It is recommended to record the batch number as well.

Hypersensitivity:

As with all injectable vaccines, appropriate medical treatment should always be available and the patient should be monitored in the event of an anaphylactic reaction following administration of the vaccine.

Precautions for use:

EFLUELDA must not be administered intravascularly under any circumstances.

Intercurrent illness:

Vaccination should be postponed in patients with acute febrile illness until fever has resolved.

Guillain-Barré syndrome:

If Guillain-Barré syndrome (GBS) occurred within 6 weeks of a previous influenza vaccination, the decision to administer EFLUELDA should be based on a careful assessment of the potential benefits and risks.

Thrombocytopenia and coagulation disorders:

As with other vaccines administered by the intramuscular route, this vaccine must be administered with caution in patients with thrombocytopenia or a coagulation disorder, as bleeding may occur following intramuscular administration in these patients.

Syncope:

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be put in place to prevent any injury due to fainting and to manage syncopal reactions.

Immunodeficiency:

The antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Protection:

As with any vaccine, a protective response may not be obtained in all vaccinated subjects.

Sodium:

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

4.5. Interaction with other medicinal products and other forms of interaction

Concomitant administration of EFLUELDA TETRA (quadrivalent influenza vaccine, 60 micrograms HA/strain) with a mRNA vaccine (modified nucleoside/elasomeran) for COVID-19 used as an investigational booster dose of 100 micrograms was evaluated in a limited number of participants in a descriptive clinical study (see sections 4.8 and 5.1).

If EFLUELDA is to be administered at the same time as other injectable vaccines, the injections should be administered on different limbs.

It should be emphasized that the undesirable effects may be intensified by any concomitant

administration.

The immune response may be reduced if the patient is receiving immunosuppressive treatment.

After influenza vaccination, false positive results were observed in serological tests using the ELISA method to detect antibodies against HIV1, hepatitis C, and in particular HTLV1. The Western Blotting technique should be used to confirm or disprove ELISA results. The transient false-positive results could be due to a non-specific IgM response induced by the vaccine.

4.6. Fertility, pregnancy and lactation

EFLUELDA is only indicated in patients aged 60 years and over.

EFLUELDA has not been clinically evaluated in pregnant or breast-feeding women.

Pregnancy

Inactivated influenza vaccines at standard doses (15 micrograms of haemagglutinin per viral strain per dose) can be used at all stages of pregnancy. The available safety data are greater for the second and third trimesters of pregnancy than for the first trimester. Global data on the use of inactivated influenza vaccines at standard doses do not indicate abnormal outcomes for the fetus and mother attributable to the vaccine. However, there are limited data on the use of 60 micrograms haemagglutinin-containing influenza vaccines for each viral strain per dose in pregnant women.

Breast-feeding

EFLUELDA can be administered during breast-feeding. Based on experience with standard-dose influenza vaccines, no effects on the breastfed infants are anticipated.

Fertility

The possible effects of EFLUELDA on human fertility have not been studied.

4.7. Effects on ability to drive and use machines

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

4.8. Undesirable effects

a. Summary of the safety profile:

EFLUELDA is identical to EFLUELDA TETRA, the only difference is that EFLUELDA contains an antigen of one strain of influenza B less. The safety profile of EFLUELDA TETRA is therefore relevant for the use of EFLUELDA. The safety of EFLUELDA TETRA was evaluated in the context of a pooled analysis of two clinical trials (QHD00013 and QHD00011) during which 2,549 subjects aged 60 years and over (378 between 60 and 64 years and 2,171 between 65 years and over) received EFLUELDA TETRA.

The most frequently reported adverse reaction after vaccination was injection site pain reported by 42.6% of participants, followed by myalgia (23.8%), headache (17.3%) and malaise (15.6%). The majority of these reactions occurred and resolved within three days of vaccination. The intensity of most of these reactions was mild to moderate.

Overall, undesirable effects were generally less common in participants aged 65 years and older than in participants aged 60 to 64 years.

The reactogenicity of EFLUELDA TETRA was slightly increased compared to the standard dose vaccine (15 micrograms of haemagglutinin of each viral strain per dose), but no major difference in intensity was observed.

The safety of EFLUELDA TETRA was evaluated during a descriptive study (QHD00028) in which subjects received either EFLUELDA TETRA concomitantly with an investigational booster dose of 100 micrograms of mRNA vaccine (modified nucleoside) against COVID-19 (n = 100) or EFLUELDA TETRA only (n = 92), or an experimental 100-microgram booster dose of the mRNA (nucleoside-modified) COVID-19 vaccine alone (n=104). The frequency and severity of local and systemic adverse reactions were similar between subjects who received the approved COVID-19 mRNA vaccine

concomitantly with EFLUELDA TETRA and subjects who received a booster dose of the approved COVID-19 mRNA vaccine.

b. Tabulated list of adverse reactions:

The data below summarize the frequency of adverse reactions reported after EFLUELDA TETRA vaccination and adverse reactions reported during clinical development and post-marketing experience of trivalent and high-dose quadrivalent influenza vaccines.

Adverse reactions are classified according to their frequency according to the following convention:

Very common ($\geq 1/10$);

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

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

Rare ($\geq 1/10\,000$ to $< 1/1\,000$);

Very rare ($< 1/10\,000$);

Not known (cannot be estimated from the available data).

ADVERSE REACTIONS	FREQUENCY
<i>General disorders and administration site conditions</i>	
Pain at the injection site, erythema at the injection site, malaise	Very common
Swelling at the injection site, induration at the injection site, bruising at the injection site, fever ($\geq 37.5^{\circ}\text{C}$), chills	Common
Injection site pruritus, fatigue	Uncommon
Asthenia	Rare
Chest pain	Not known*
<i>Musculoskeletal and systemic disorders</i>	
Myalgia	Very common
Muscle weakness ^a	Uncommon
Arthralgia, pain in the extremities	Rare
<i>Nervous system disorders</i>	
Headaches	Very common
Lethargy ^a	Uncommon
Dizziness, paraesthesia	Rare
Guillain-Barré syndrome (GBS), seizures, febrile seizures, myelitis (including encephalomyelitis and transverse myelitis), facial paralysis (Bell's paralysis), optic neuropathy/neuropathy, brachial neuritis, syncope (rapidly after vaccination)	Not known*
<i>Blood and lymphatic system disorders</i>	
Thrombocytopenia, lymphadenopathy	Not known*
<i>Respiratory, thoracic and mediastinal disorders</i>	
Cough, oropharyngeal pain	Uncommon
Rhinorrhoea	Rare
Dyspnoea, wheezing, tight throat	Not known*
<i>Gastrointestinal disorders</i>	

Nausea, vomiting, dyspepsia, ^a diarrhoea	Uncommon
<i>Immune system disorders</i>	
Pruritus, urticaria, night sweats, rash	Rare
Anaphylactic reactions, other allergic/hypersensitivity reactions (including angioedema)	Not known*
<i>Vascular disorders</i>	
Redness	Rare
Vasculitis, vasodilation	Not known*
<i>Ear and labyrinth disorders</i>	
Vertigo	Rare
<i>Eye disorders</i>	
Ocular hyperaemia	Rare

^a Dyspepsia, lethargy and muscle weakness were observed with EFLUELDA during the QHD00013 trial.

* Reported during post-marketing experience with EFLUELDA and EFLUELDA TETRA

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 according to the National Regulation by using an online form <https://sideeffects.health.gov.il/>.

4.9. Overdose

Cases of administration of a higher dose than the recommended dose (overdose) have been reported with EFLUELDA, during accidental use in the population under 60 years of age due to a medication error. When undesirable effects were reported, they corresponded to the known safety profile of EFLUELDA (see section 4.8).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02.

Influenza vaccination is recommended annually because of the duration of immunity conferred by the vaccine and because the circulating strains of influenza viruses may change from one year to another.

Clinical efficacy

FIM12 is a multicentre, double-blind clinical efficacy trial conducted in the United States and Canada in which adults aged 65 years and over were randomized (1:1) to receive EFLUELDA or the trivalent vaccine at standard dose. The study was conducted during two influenza seasons (2011-2012 and 2012-2013) to assess the occurrence of laboratory-confirmed influenza caused by any influenza virus type/subtype, associated with influenza-like illness, as a primary endpoint.

Participants were followed-up to detect the onset of respiratory disease through active and passive monitoring, starting 2 weeks after vaccination and for approximately 7 months. After an episode of respiratory disease, nasopharyngeal swab samples were analysed; influenza attack rates and vaccine efficacy were measured. The predefined statistical superiority criterion for the primary endpoint (lower limit of the two-sided 95% CI of the efficacy of EFLUELDA compared to the standard dose vaccine >9.1%) was met.

Table 3: Relative efficacy of the vaccine to prevent laboratory-confirmed influenza associated with influenzapal^a syndrome in adults aged 65 years and over

	Trivalent high-dose vaccine (TIV-HD) N ^b = 15,892 n ^c (%)	Trivalent vaccine standard dose N ^b = 15,911 n ^c (%)	Relative efficacy % (95% CI)
Laboratory-confirmed influenza ^d caused by:			
Any type/subtype of influenza virus^e	227 (1.43)	300 (1.89)	24.2 (9.7; 36.5)
Viral strains similar to those contained in the vaccine	73 (0.46)	113 (0.71)	35.3 (12.4; 52.5)

^a Influenza syndrome: onset of at least one of the following respiratory symptoms: irritated throat, cough, production of sputum, wheezing, or difficulty breathing; associated simultaneously with at least one of the following general signs or symptoms: temperature >37.2°C, chills, fatigue, headache or myalgia.

^b N is the number of vaccinated participants subject to the per-protocol analysis for the evaluation of efficacy.

^c n is the number of participants with protocol-defined and laboratory-confirmed influenza syndrome.

^d Confirmed in the laboratory: by culture or by polymerase chain reaction

^e Primary endpoint

Immunogenicity

Immunogenicity study comparing EFLUELDA to a standard dose vaccine in adults aged 65 years and over: FIM05

A phase 3, multicentre, randomized, controlled, double-blind, active comparator study was conducted in the United States in adults aged 65 years and over to demonstrate the superiority of EFLUELDA compared to the standard dose vaccine, assessed by seroconversion rates and Geometric Means of Antibody Titre (GMT) ratios. A total of 3,876 adults were randomized to receive either one dose of EFLUELDA or one dose of the vaccine at the standard dose.

EFLUELDA induced a higher immune response for the A/H1N1 and A/H3N2 strains and a non-inferior immune response for the B strain, both in terms of GMT ratios and seroconversion rate 28 days after vaccination, compared to the standard dose vaccine.

Immunogenicity study comparing EFLUELDA to EFLUELDA TETRA in adults aged 65 years and over: QHD00013

A phase 3, randomized, double-blind, active comparator-controlled clinical study was conducted in the United States in adults aged 65 years and over to demonstrate the non-inferiority of EFLUELDA TETRA compared to EFLUELDA, by comparing the geometric mean of antibody titres (GMT) measured by haemagglutination inhibition (HAI) on 28 days after vaccination (serovaccination).

In total, 2,670 adults were randomized to receive either a dose of EFLUELDA TETRA or a dose of EFLUELDA (one of the two formulations of the comparator vaccine, containing either a B strain of the Yamagata lineage or a B strain of the Victoria lineage).

EFLUELDA TETRA was as immunogenic as EFLUELDA for GMTs measured by haemagglutination inhibition (HAI) and seroconversion rates for common influenza strains.

These data make it possible to extrapolate the immunogenicity, efficacy and real-life efficacy results of EFLUELDA TETRA to EFLUELDA.

Immunogenicity study comparing high-dose influenza vaccine with standard-dose influenza vaccine in adults aged 60 years and over: Trial QHD00011

A phase 3, randomized, controlled, double-blind, active *comparator* clinical trial was conducted in Europe in people aged 60 years and older to demonstrate the superiority of EFLUELDA TETRA compared to a standard dose vaccine for all strains, by comparing the geometric mean antibody titres (GTM) measured by inhibition of haemagglutination (HAI) at Day 28 in adults aged 60 to 64 years and in adults aged 65 years and older.

In total, 1,539 people (760 aged between 60 and 64 years and 779 aged 65 years and over) were

randomized to receive either a dose of EFLUELDA TETRA or a dose of the standard dose influenza vaccine.

EFLUELDA TETRA induced an immune response greater than the immune responses induced by the influenza vaccine at a standard dose for the 4 strains of viruses 28 days after vaccination in adults aged 60 to 64 years, and this response was at least similar to the immune response observed in adults aged 65 years and older. Clinical and real-life efficacy data from 65 years of age can therefore be inferred for adults from 60 years of age.

Real-life efficacy studies:

A controlled, randomized, clustered clinical study conducted in nursing homes in the United States evaluated the relative efficacy of EFLUELDA, compared to the trivalent vaccine at standard dose in the prevention of hospitalization among 53,008 individuals during the influenza season 2013-2014.

During the 2013-2014 season, the incidence of respiratory-related hospitalizations (primary endpoint) was significantly reduced by 12.7% (adjusted relative risk [ARR] = 0.873, 95% CI: 0.776; 0.982, $p=0.023$) in institutions where the residents received EFLUELDA compared to those who received a standard dose influenza vaccine. In addition, with regard to the secondary endpoints, EFLUELDA reduced hospitalizations for pneumonia by 20.9% (ARR 0.791, 95% CI: 0.267; 0.953, $p=0.013$) and hospitalizations for all causes (ARR = 0.915, 95% CI: 0.863; 0.970, $p=0.0028$) compared to a standard dose influenza vaccine.

Several retrospective studies, performed during 11 influenza seasons and in more than 45 million people aged 65 years and over, have confirmed the superiority of the EFLUELDA protection compared to the standard dose influenza vaccine, against influenza complications such as hospitalizations for influenza or pneumonia (13,4% (95% CI: 7.3%; 19,2%, $p<0,001$)), hospitalizations for cardiovascular or respiratory events (17,9% (95% CI: 14,7%; 21,0%, $p<0,001$)) and hospitalizations “all causes” (7,8% (95% CI: 5,3%; 10,3%, $p<0,001$)); even if the impact may vary depending on the season.

Concomitant administration of EFLUELDA TETRA with the mRNA (modified nucleoside) vaccine against COVID-19

During an open-label descriptive clinical study (NCT04969276), adults aged 65 years and over, in good health, were divided into three groups: Group 1 received EFLUELDA TETRA alone (N=92), Group 2 (N=100) received EFLUELDA TETRA concomitantly with an experimental booster dose of 100 micrograms of the mRNA (modified nucleoside) vaccine against COVID-19 at least 5 months after the second dose of the primary vaccination, Group 3 (N = 104) only received the investigational booster dose of 100 micrograms of the mRNA (modified nucleoside) vaccine against COVID-19.

Co-administration did not cause any change in immune responses to the influenza vaccine, as measured by the haemagglutination inhibition test (HAI). Co-administration led to similar responses to the COVID-19 mRNA vaccine, assessed by an anti-spike IgG assay (see sections 4.5 and 4.8).

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 local tolerability and repeated dose toxicity.

The carcinogenic or mutagenic potential of EFLUELDA and its effects on reproductive and developmental functions have not been evaluated.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Sodium phosphate-buffered isotonic sodium chloride solution with:
 - Sodium chloride
 - Dibasic sodium phosphate

- Monobasic sodium phosphate
- Water for injection
- Octoxinol-9

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product 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 (2°C – 8°C). Do not freeze. Keep the syringe in the outer carton in order to protect from light.

6.5. Nature and contents of container

0.5 ml of suspension in pre-filled syringes (type I glass) with a plunger stopper (bromobutyl elastomer) and protective cap.

Box of 1, 5 or 10 pre-filled syringe(s) without needles.

Box of 1, 5 or 10 pre-filled syringe(s) with separate needle(s) (stainless steel).

Box of 1 or 10 pre-filled syringe(s) with separate needle(s) (stainless steel) with a safety shield (polycarbonate).

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

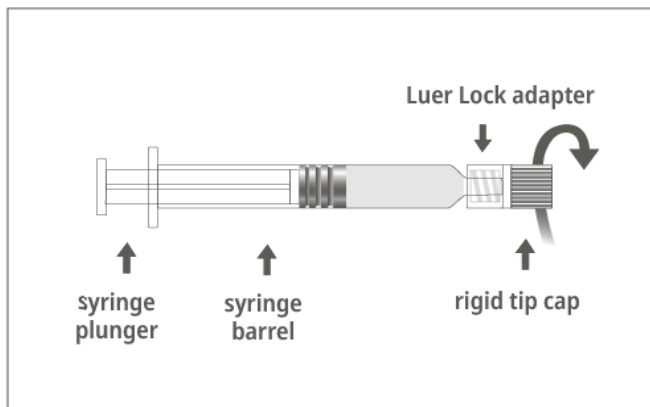
The vaccine should be brought to room temperature before use. Shake before use.

The vaccine should be visually inspected for particulate matter and/or a change in colour before administration whenever the solution and packaging allow it. The vaccine should not be used if particles or a change in colour are observed.

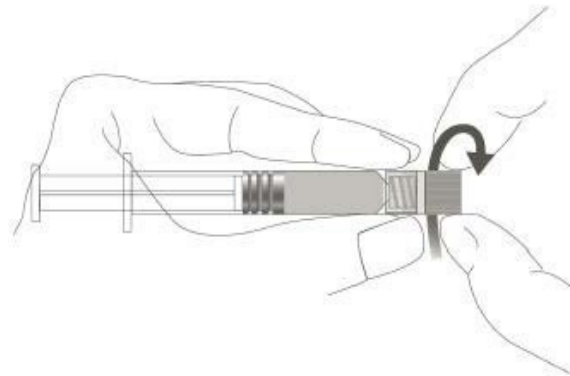
Preparation for administration:

The pre-filled syringe may be supplied with a Luer Lock and a rigid (Figure A) or soft protective cap (Figure D). The syringe containing the suspension for injection must be visually inspected before administration. If there are foreign particles, leakage, premature activation of the plunger or defective nozzle, discard the prefilled syringe.

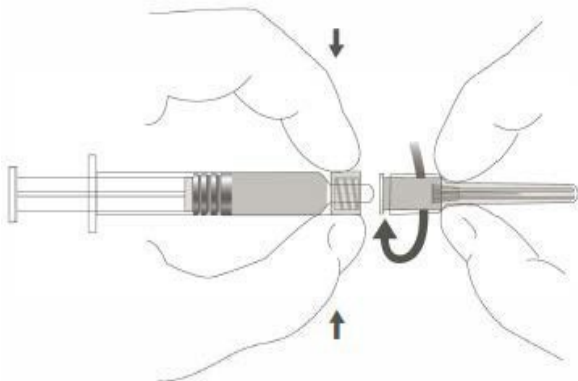
Figure A: Luer Lock syringe with a rigid protective cap



Step 1: While holding the Luer Lock adapter with one hand (avoid holding the plunger or the syringe barrel), twist the protective cap off.

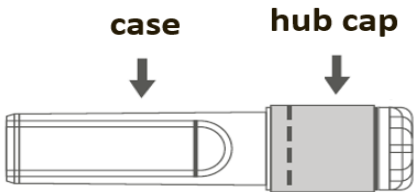
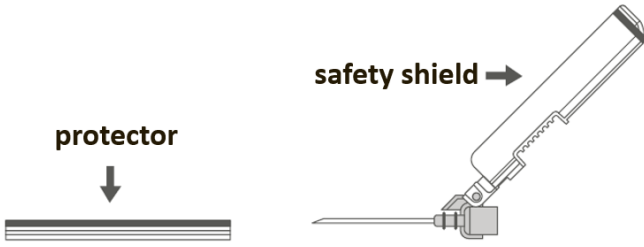
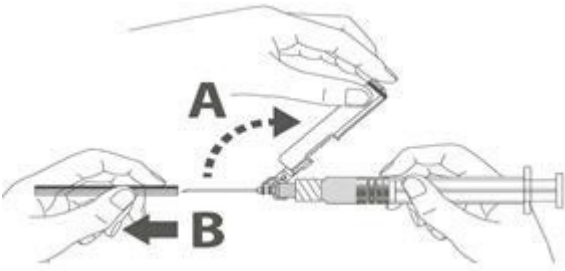
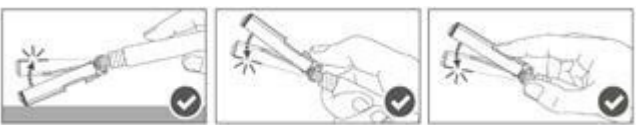
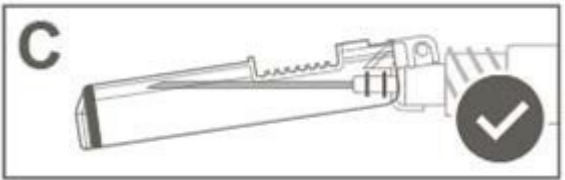
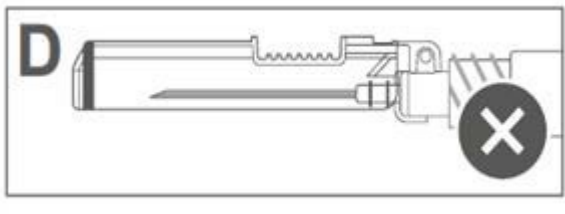


Step 2: To attach the needle to the syringe, gently screw the needle onto the Luer Lock adapter until slight resistance is felt.



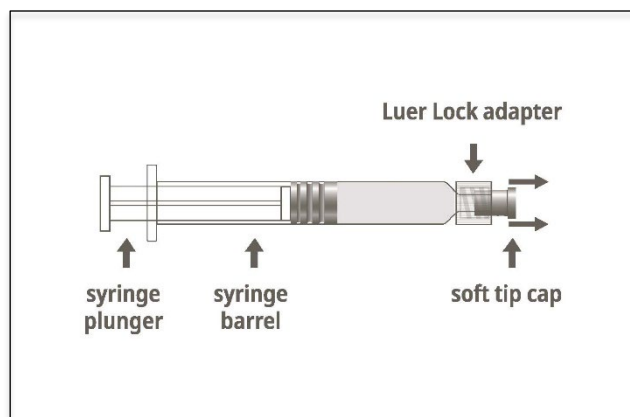
Instructions for using the safety needle with the pre-filled Luer Lock syringe:

Follow Steps 1 and 2 above to prepare the Luer Lock syringe and needle attachment.

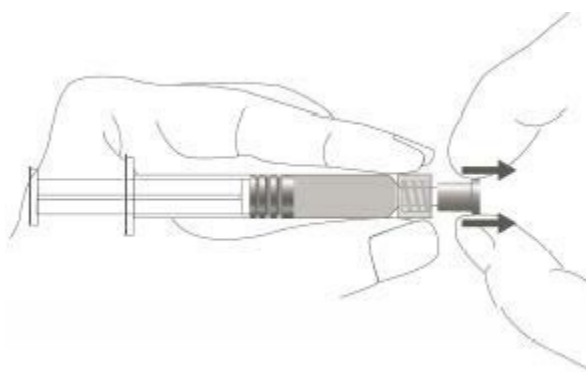
Figure B: Secure needle (inside case)	Figure C: Safety needle components (prepared for use)
	
Step 3: Remove the cap from the secured needle by pulling straight out. The needle is covered by the safety shield and the needle guard.	
Step 4: A: Lift the safety shield by pulling it away from the needle and towards the syringe body at the indicated angle. B: Pull the needle guard straight out.	
Step 5: Once the injection is complete, the safety shield should be locked (activated) with one hand using one of the three (3) techniques shown: activation using a surface, thumb or index finger. Comment: Activation is verified by an audible and/or tactile “click”.	
Step 6: Visually inspect the activation of the safety shield. The safety shield must be fully locked (activated) as shown in Figure C.	
Figure D indicates that the safety shield is NOT fully locked (not activated) .	

Caution: Do not attempt to unlock (deactivate) the safety device by forcing the needle out of the safety shield.

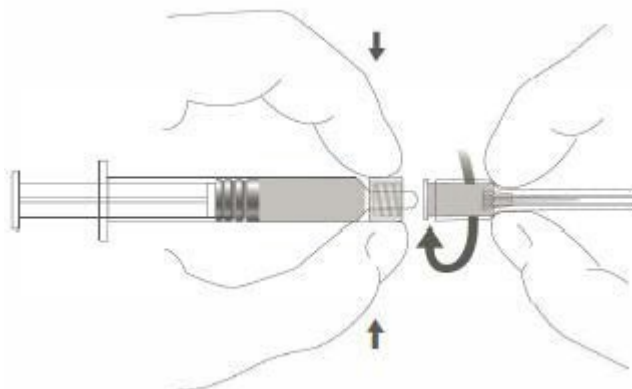
Figure D: Luer Lock syringe with a soft protective cap



Step 1: While holding the Luer Lock adapter with one hand (avoid holding the plunger or the syringe barrel), remove the soft protective cap.



Step 2: To attach the needle to the syringe, gently screw the needle to the Luer Lock adapter until slight resistance is felt.



The syringe is intended for single use only and must not be reused. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

182-57-38440-00

Approved in June 2026.