Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Efluelda suspension for injection in pre-filled syringe Trivalent influenza vaccine (split virion, inactivated), 60 micrograms HA/strain

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

A/Victoria/4897/2022 (H1N1)pdm09-like strain
(A/Victoria/4897/2022, IVR-238)..... 60 micrograms HA**

A/Croatia/10136RV/2023 (H3N2)-like strain
(A/Croatia/10136RV/2023, X-425A)..... 60 micrograms HA**

B/Austria/1359417/2021-like strain
(B/Michigan/01/2021, wild type)..... 60 micrograms HA**
Per 0.5 ml dose

* propagated in embryonated chicken eggs
** haemagglutinin

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

Efluelda may contain traces of eggs, such as ovalbumin, formaldehyde which are 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 syringe (Suspension for injection)
Efluelda after shaking gently, is a colourless opalescent liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Efluelda is indicated for active immunisation in adults 60 years of age 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 adults 60 years of age and older: one dose of 0.5 ml.

Paediatric population
The safety and effectiveness of Efluelda in children less than 18 years of age have not been established.

Method of administration
The preferred route of administration for this vaccine is intramuscular although it may also be given subcutaneously.

The recommended site for intramuscular injection is the deltoid region. The vaccine should not be injected into the gluteal region, or into areas where there may be a major nerve trunk.

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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.

Hypersensitivity
As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Precaution for use
Efluelda should under no circumstances be administered intravascularly.

Intercurrent illness
Vaccination should be postponed in patients with acute febrile illness until the fever is resolved.

Guillain-Barré syndrome
If Guillain-Barré syndrome (GBS) has occurred within 6 weeks of any previous influenza vaccination, the decision to give Efluelda should be based on careful consideration of the potential benefits and risks.

Thrombocytopenia and coagulation disorders
As with other vaccines administered intramuscularly, the vaccine should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

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

Immunodeficiency
Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Protection
As with any vaccine, a protective response may not be elicited in all vaccine recipients.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium free".

4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of Efluelda Tetra (Quadrivalent Influenza Vaccine High-Dose) with an investigational booster 100 mcg dose of COVID-19 mRNA vaccine (nucleoside modified/elasomeran) has been evaluated in a limited number of participants in a descriptive clinical study (see sections 4.8 and 5.1).

If Efluelda needs to be given at the same time as another injectable vaccine(s), immunisation should be carried out on separate limbs.

It should be noted that the adverse reactions may be intensified by any co-administration.

The immunological response may be reduced if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been reported. An appropriate Western Blot test should be used to confirm or disprove the results of the ELISA test. The transient false positive reactions could be due to a non-specific IgM response induced by influenza vaccine.

4.6 Fertility, pregnancy and lactation

Efluelda is only indicated for use in adults aged 60 years and older.
Efluelda has not been clinically evaluated in pregnant and breast-feeding women.
Pregnancy
Inactivated influenza standard dose vaccines (15 micrograms haemagglutinin of each virus strain per dose) can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester. Data from worldwide use of inactivated influenza standard dose vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine. However, data on the use of influenza vaccines containing 60 micrograms haemagglutinin of each virus strain per dose in pregnant women are limited.

Breastfeeding
Efluelda may be used during breast-feeding. Based on experience with standard dose vaccines, no effects on the breast-fed infant are anticipated.

Fertility
Efluelda has not been evaluated for possible effects on human fertility.

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 with the only difference of containing antigen from one less influenza B strain. The safety profile of Efluelda Tetra is therefore relevant to the use of Efluelda.

The safety of Efluelda Tetra was assessed in a pooled analysis of two clinical trials (QHD00013 and QHD00011) in which 2549 adults from 60 years of age and older (378 adults from 60 to 64 years of age and 2171 adults 65 years of age and older) received Efluelda Tetra.

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

Overall, adverse reactions were generally less frequent in participants aged 65 years and older than in participants aged 60 to 64 years.

Reactogenicity of Efluelda Tetra was slightly increased as compared to the standard dose vaccine (15 micrograms haemagglutinin of each virus strain per dose), but no major difference in intensity was observed.

The safety of Efluelda Tetra was evaluated in a descriptive study (QHD00028) in which subjects received Efluelda Tetra together with an investigational booster 100 mcg dose of COVID-19 mRNA vaccine (nucleoside modified) (n=100), Efluelda Tetra only (n=92) or an investigational booster 100 mcg dose of COVID-19 mRNA vaccine (nucleoside modified) only (n=104). The frequency and severity of local and systemic adverse reactions was similar in subjects who were co-administered with Efluelda Tetra and licensed COVID-19 mRNA vaccine and subjects administered with a booster dose of licensed COVID-19 mRNA vaccine.

b Tabulated list of adverse reactions

The data below summarizes the frequencies of adverse reactions that were recorded following vaccination with Efluelda Tetra and adverse reactions reported during clinical development and post-marketing experience with the trivalent and the quadrivalent influenza high-dose vaccines.

Adverse events 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 available data).

ADVERSE REACTIONS	**FREQUENCY**
General Disorders and Administration Site Conditions	
Injection site pain, injection site erythema, malaise	Very common
Injection site swelling, injection site induration, injection site bruising, fever (≥37.5 °C), shivering	Common
Injection site pruritis, fatigue	Uncommon
Asthenia	Rare
Chest pain	Not known*
Musculoskeletal and Connective Tissue Disorders	
Myalgia	Very common
Muscle weakness[a]	Uncommon
Arthralgia, pain in extremities	Rare
Nervous System Disorders	
Headache	Very common
Lethargy[a]	Uncommon
Dizziness, paraesthesia	Rare
Guillain-Barré syndrome (GBS), convulsions, febrile convulsions, myelitis (including encephalomyelitis and transverse myelitis), facial palsy (Bell's palsy), optic neuritis/neuropathy, brachial neuritis, syncope (shortly after vaccination)	Not known*
Blood and Lymphatic System Disorders	
Thrombocytopenia, lymphadenopathy	Not known*
Respiratory, Thoracic and Mediastinal Disorders	
Cough, oropharyngeal pain	Uncommon
Rhinorrhoea	Rare
Dyspnoea, wheezing, throat tightness	Not known*
Gastrointestinal Disorders	
Nausea, vomiting, dyspepsia[a], diarrhoea	Uncommon
Immune System Disorders	
Pruritus, urticaria, night sweats, rash	Rare
Anaphylaxis, other allergic/hypersensitivity reactions (including angioedema)	Not known*
Vascular Disorders	
Flushing	Rare
Vasculitis, vasodilatation	Not known*
Ear and Labyrinth Disorders	
Vertigo	Rare
Eye Disorders	
Ocular hyperaemia	Rare

[a] Dyspepsia, lethargy, and muscular weakness were observed with Efluelda in the QHD00013 trial.
* Reported during post-marketing experience with Efluelda or 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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Cases of administration of more than the recommended dose have been reported with Efluelda associated with inadvertent use in the population below 60 years of age due to medication error. When adverse reactions were reported, the information was consistent with the known safety profile of Efluelda (see section 4.8).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02.
Annual influenza vaccination is recommended because immunity during the year after vaccination declines and because circulating strains of influenza virus change from year to year.

Clinical Efficacy
FIM12 was a multi-centre, double-blind efficacy trial conducted in the US and Canada in which adults 65 years of age and older were randomised (1:1) to receive the Efluelda or a standard dose vaccine. The study was conducted over two influenza seasons (2011-2012 and 2012-2013) to assess the occurrence of laboratory-confirmed influenza caused by any influenza viral type/subtype, in association with influenza-like illness (ILI) as the primary endpoint.

Participants were monitored for the occurrence of a respiratory illness by both active and passive surveillance, starting 2 weeks post-vaccination for approximately 7 months. After an episode of respiratory illness, nasopharyngeal swab samples were collected for analysis; attack rates and vaccine efficacy were calculated. The pre-specified statistical superiority criterion for the primary endpoint (lower limit of the 2-sided 95% CI of the vaccine efficacy for the Efluelda relative to standard dose vaccine > 9.1%) was met.

Table 3: Relative vaccine efficacy to prevent influenza-like illness[a] in adults ≥ 65 years

	High Dose vaccine N[b]=15892 n[c] (%)	**Standard dose vaccine N[b]=15911 n[c] (%)**	**Relative Efficacy % (95% CI)**
Laboratory-confirmed influenza[d] caused by:			
• **Any type/subtype[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] Occurrence of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature >37.2 °C, chills, tiredness, headaches or myalgia
[b] N is the number of vaccinated participants in the per-protocol analysis set for efficacy assessments
[c] n is the number of participants with protocol-defined influenza-like illness with laboratory confirmation
[d] Laboratory-confirmed: culture- or polymerase-chain-reaction-confirmed
[e] Primary endpoint

Immunogenicity

Immunogenicity study comparing Efluelda with a standard dose vaccine in adults 65 years and older: FIM05
A phase 3 randomised, double-blind, active-controlled, multi-centre trial was conducted in US in adults aged 65 years and older to demonstrate the superiority of the Efluelda versus a standard dose vaccine, as assessed by seroconversion rates and GMT ratios. A total of 3,876 adults were randomised to receive either one dose of Efluelda or standard dose vaccine.
Efluelda induced superior immune response against A/H1N1 and A/H3N2 strains and a non-inferior immune response against B strain, both in terms of GMT ratios and seroconversion rates 28 days after vaccination, compared to standard dose vaccine.

Immunogenicity study comparing Efluelda with Efluelda Tetra in adults 65 years and older: QHD00013
A randomised, active-controlled, modified double-blind Phase III clinical trial was conducted in the U.S. in adults 65 years and older to demonstrate the noninferiority of Efluelda Tetra over Efluelda as assessed by HAI (haemagglutinin inhibition) Geometric mean antibody titres (GMTs) at Day 28 and seroconversion rates.
A total of 2670 adults were randomised to receive either one dose of Efluelda Tetra or one dose of Efluelda (one of two formulations of 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 HAI GMTs and seroconversion rates for the common influenza strains. These data allow extrapolating the immunogenicity, efficacy and effectiveness results of Efluelda Tetra to Efluelda.

Immunogenicity study comparing High dose Influenza vaccine with Standard dose influenza vaccine in adults 60 years and older: QHD00011
A randomised, active-controlled, modified double-blind, Phase III clinical trial was conducted in Europe in adults 60 years and older to demonstrate the superiority of Efluelda Tetra over Standard dose influenza vaccine for all strains, as assessed by HAI (haemagglutinin inhibition) geometric mean antibody titres (GMTs) at Day 28 in adults 60 to 64 years of age and in adults 65 years of age and older.

A total of 1539 adults (760 adults 60 to 64 years of age and 779 adults 65 years of age and older) were randomised to receive either one dose of Efluelda Tetra or one dose of Standard dose influenza vaccine.

Efluelda Tetra induced a superior immune response to Standard dose influenza vaccine for all 4 virus strains 28 days post-vaccination in adults 60 to 64 years of age, and this response was at least similar to the immune response in adults 65 years and above. The efficacy and effectiveness data from 65 years of age and above can thus be inferred to adults from 60 years of age and above.

Effectiveness Studies
A cluster-randomised, controlled clinical trial in United States nursing homes assessed the relative effect of Efluelda versus a standard dose of influenza vaccine in hospitalizations among 53008 individuals during the 2013-2014 influenza season.

During the 2013-2014 season, the incidence of respiratory-related hospital admissions (primary objective) was significantly reduced in facilities where residents received Efluelda compared with those that received standard-dose influenza vaccines by 12.7% (adjusted risk ratio [ARR] 0.873, 95% CI 0.776 to 0.982, p=0.023). Moreover, with respect to secondary endpoints, Efluelda reduced hospital admissions for pneumonia by 20.9% (ARR 0.791, 95% CI: 0.267 to 0.953, p=0.013) and all-cause hospital admissions by 8% (ARR 0.915, 95% CI: 0.863 to 0.970, p=0.0028).

Several retrospective studies, over 11 influenza seasons and in more than 45 million individuals 65 years of age and older, confirmed the superior protection offered by Efluelda compared to standard-dose influenza vaccines against complications of influenza such as pneumonia and influenza hospitalization (13.4% (95%CI: 7.3% to 19.2%, p<0.001)), cardio-respiratory hospitalizations 17.9% (95%CI :14.7% to 21.0%, p<0.001) and all –cause hospitalization 7.8% (95%CI: 5.3% to 10.3%, p<0.001) ; although the impact may vary per season.

Concomitant Administration of Efluelda Tetra with COVID-19 mRNA Vaccine (nucleoside modified)
In a descriptive open-label clinical study (NCT04969276), healthy adults aged 65 years and older were divided in three groups: Group 1 received Efluelda Tetra alone (N=92), Group 2 (N=100) received Efluelda Tetra concomitantly with an investigational booster 100 mcg dose of COVID-19 mRNA vaccine (nucleoside modified) at least 5 months after the second dose of the primary series, Group 3 (N=104) received only the investigational booster 100 mcg dose of COVID-19 mRNA vaccine (nucleoside modified).
Co-administration resulted in no change to influenza vaccine immune responses as measured by haemagglutination inhibition (HAI) assay. Co-administration resulted in similar responses to COVID-19 mRNA vaccine, as assessed by an anti-spike IgG assay (see section 4.5 and 4.8).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Nonclinical data reveal no special hazards for humans based on conventional studies of local tolerance and repeated dose toxicity studies.

Efluelda has not been evaluated for carcinogenic or mutagenic potential nor for developmental and reproductive toxicity study.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium phosphate-buffered isotonic sodium chloride solution
    - Sodium chloride,
    - Monobasic sodium phosphate
    - Dibasic sodium phosphate
    - Water for injections
- 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

12 months

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 syringe (Type I glass) equipped with a plunger stopper (bromobutyl rubber) and a tip-cap.
Pack of 1, 5 or 10 pre-filled syringe(s) without needle(s).
Pack of 1, 5 or 10 pre-filled syringe(s) with separate needle(s) (stainless steel).
Pack of 1 or 10 pre-filled syringe(s) with separate needle(s) (stainless steel) with safety shield (polycarbonate).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

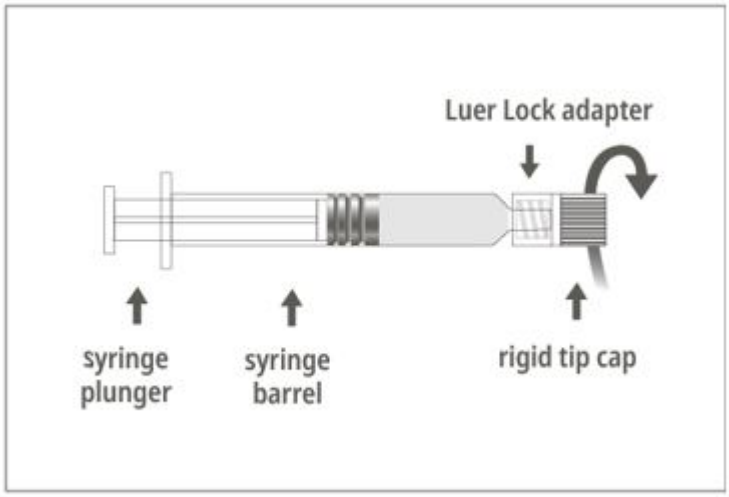
The vaccine should be allowed to reach room temperature before use.

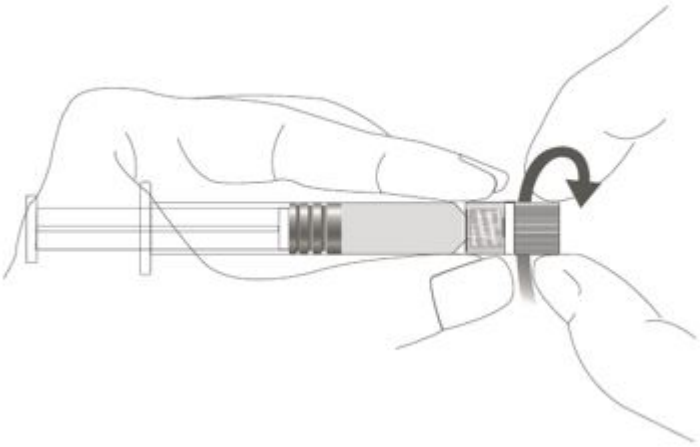
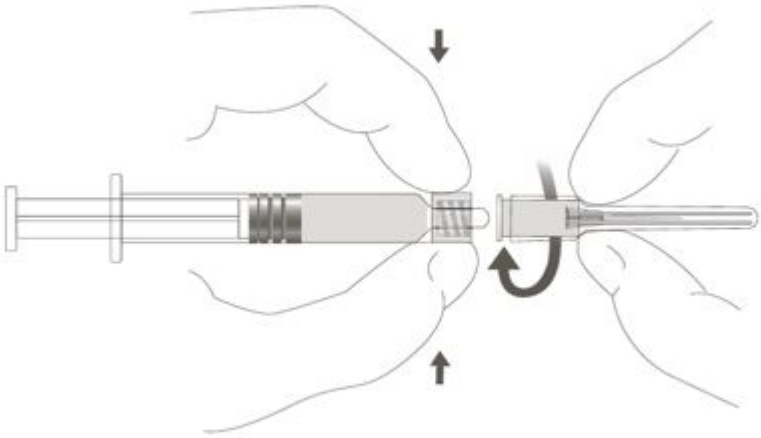
Shake before use.

The vaccines should be inspected visually for particulate matter and/or discoloration prior to administration whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered.

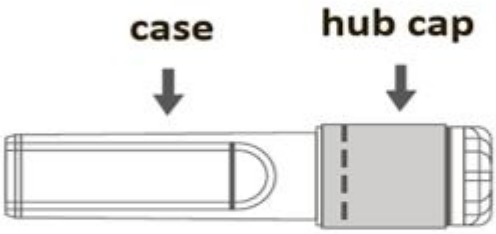
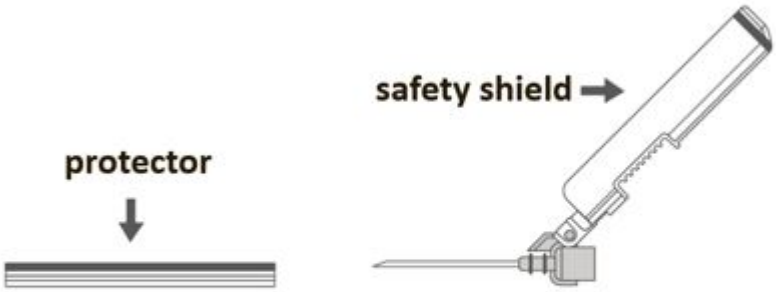
Preparation for Administration

The pre-filled syringe can be supplied with a Luer Lock with either Rigid Tip Cap (Picture A) or Soft Tip Cap (Picture D). The syringe with suspension for injection should be visually inspected prior to administration. In the event of any foreign particulate matter, leakage, premature activation of the plunger or faulty tip seal, discard the pre-filled syringe.
Picture A: Luer Lock Syringe with Rigid Tip Cap

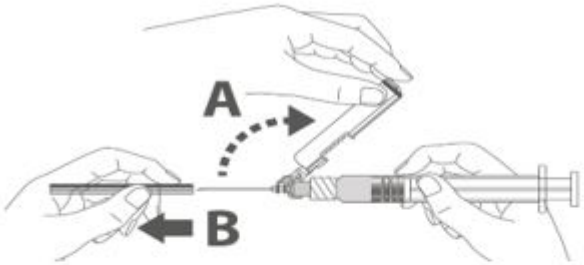
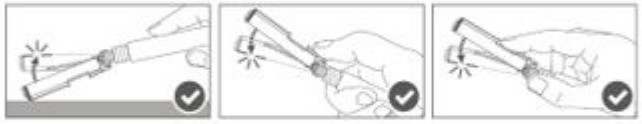
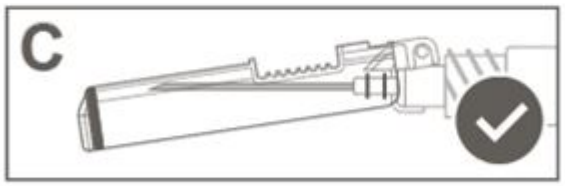
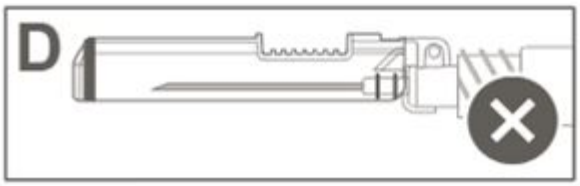


Step 1: Holding the Luer Lock adapter in one hand (avoid holding the syringe plunger or barrel), unscrew the tip cap by twisting it.	
Step 2: To attach the needle to the syringe, gently twist the needle into the Luer Lock adapter of the syringe until slight resistance is felt.	

Instructions for use of Safety Needle with Luer Lock pre-filled syringe:
Follow Step 1 and 2 above to prepare the Luer Lock syringe and needle for attachment.

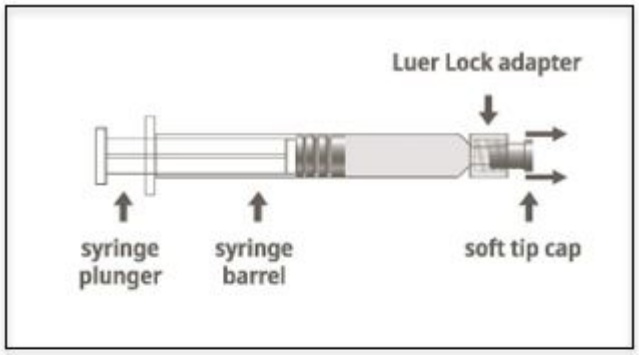
Picture B: Safety Needle (inside case)	Picture C: Safety Needle Components (prepared for use)
	

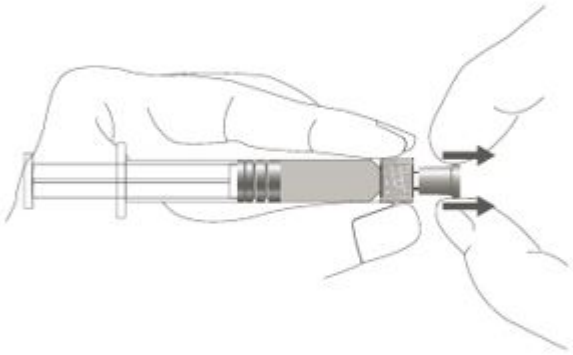
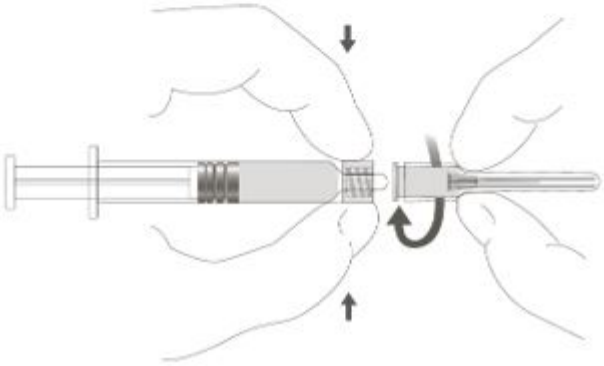
Step 3: Pull the safety needle's case straight off. The needle is covered by the safety shield and protector.

Step 4: **A:** Move the safety shield away from the needle and toward the syringe barrel to the angle shown. **B:** Pull the protector straight off.	
Step 5: After injection is complete, lock (activate) the safety shield using one of the three (3) **one-handed** techniques illustrated: surface, thumb or finger activation. Note: Activation is verified by an audible and/or tactile "click."	
Step 6: Visually inspect the safety shield activation. The safety shield should be **fully locked (activated)** as shown in Figure C. Figure D shows 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.

Picture D: Luer Lock Syringe with Soft Tip Cap



Step 1: Holding the Luer Lock adapter in one hand (avoid holding the syringe plunger or barrel), pull-off the tip cap.	
Step 2: To attach the needle to the syringe, gently twist the needle into the Luer Lock adapter of the syringe until slight resistance is felt.	

The syringe is intended for single use onlyand 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 Winthrop Industrie
82 Avenue Raspail
Gentilly
94250
France

8 MARKETING AUTHORISATION NUMBER

PA23458/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th November 2024

10 DATE OF REVISION OF THE TEXT

February 2026