1. NAME OF THE MEDICINAL PRODUCT

FLUARIX

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)
15 micrograms HA**
A/Croatia/10136RV/2023 (H3N2)-like strain (A/Croatia/10136RV/2023, X-425A)
15 micrograms HA**
B/Austria/1359417/2021-like strain (B/Austria/1359417/2021, BVR-26)
15 micrograms HA**

per 0.5 ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks
** haemagglutinin

This vaccine complies with the World Health Organisation (WHO) recommendation (northern hemisphere) and EU recommendation for the **2025/2026** season.

Fluarix may contain traces of ovalbumin, hydrocortisone, gentamicin sulphate, formaldehyde and sodium deoxycholate which are used during the manufacturing process (see section 4.3).

Excipient with known effect

The vaccine contains not more than 0.415 mg of polysorbate 80 per dose (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.
The suspension is colourless and slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fluarix is indicated for active immunisation of adults and children from 6 months of age for the prevention of influenza disease caused by the two influenza A virus subtypes and one influenza B virus lineage contained in the vaccine .

The use of Fluarix should be based on official recommendations.

4.2 Posology and method of administration

Posology

Adults

One dose of 0.5 ml.

Paediatric population

Children from 6 months to 17 years of age: One dose of 0.5 ml.

Children 6 months to less than 9 years of age who have not previously been vaccinated, should be given a second dose of 0.5 ml after an interval of at least 4 weeks.

The safety and efficacy of Fluarix in children less than 6 months have not been established.

Method of administration

Fluarix administration should be carried out by intramuscular injection, preferably into the deltoid muscle or anterolateral thigh (depending on the muscle mass).

Precautions to be taken before handling or administering the medicinal product

For instructions on the 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 ovalbumin, hydrocortisone, gentamicin sulphate, formaldehyde and sodium deoxycholate.

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.

Prior to immunisation

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

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

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

As with other vaccines, vaccination with Fluarix should be postponed in individuals suffering from acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in deferral of vaccination.

Fluarix is intended to provide protection against those strains of virus from which the vaccine is prepared and to closely related strains. Fluarix may not be effective against all possible strains of influenza virus.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

Precautions for use

Fluarix should not be administered intravascularly.

As with other vaccines administered intramuscularly, Fluarix should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

Systemic immunosuppressive medications and immunodeficiency

It may be expected that in patients receiving immunosuppressive treatment or persons with immunodeficiency, an adequate immune response may not be elicited.

Interference with serological testing

False positive ELISA serologic tests for HIV-1, Hepatitis C, and especially HTLV-1 may occur following influenza vaccination. These transient false-positive results may be due to cross-reactive IgM elicited by the vaccine. For this reason, a definitive diagnosis of HIV-1, Hepatitis C, or HTLV-1 infection requires a positive result from a virus-specific confirmatory test (e.g. Western Blot or immunoblot or PCR).

Excipients

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

This medicinal product contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium-free'.

This medicinal product contains not more than 0.415 mg of polysorbate 80 per dose. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of vaccines has been evaluated in studies conducted with Fluarix Tetra (quadrivalent influenza vaccine).

If Fluarix is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

Data showing that Fluarix can be administered concomitantly with other vaccines are available for the following vaccines: pneumococcal polysaccharide vaccine (in subjects aged 50 years and above), adjuvanted herpes zoster vaccine (Shingrix) or coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccines (see section 5.1).

The frequency of injection site pain reported in subjects vaccinated concomitantly with Fluarix Tetra and 23-valent pneumococcal polysaccharide vaccine (PPV23) is similar to that observed with PPV23 alone, and higher compared to Fluarix Tetra alone.

Incidence of fatigue, headache, myalgia, arthralgia, gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain), and shivering reported in subjects vaccinated concomitantly with Fluarix Tetra and Shingrix is higher compared to Fluarix Tetra alone.

Incidence of solicited adverse events reported in subjects vaccinated concomitantly with Fluarix Tetra and COVID-19 mRNA is similar to that observed with COVID-19 mRNA alone, and higher compared to Fluarix Tetra alone.

4.6 Fertility, pregnancy and lactation

Pregnancy

Inactivated influenza vaccines, such as Fluarix, can be given in any stage of pregnancy. Larger safety datasets are available on vaccine use during the second or third trimester, compared with the first trimester.

The safety of Fluarix when administered to pregnant women has not been evaluated in clinical trials. Available post-marketing data on Fluarix do not indicate an increased risk of adverse pregnancy outcomes.

Animal studies with Fluarix do not indicate direct or indirect harmful effects with respect to reproductive and developmental toxicity (see section 5.3).

The safety data from worldwide use and systematic literature review for inactivated seasonal influenza vaccines administered during pregnancy do not indicate an increased risk of any adverse foetal and maternal outcomes attributable to the vaccine.

Breast-feeding

It is unknown whether Fluarix is excreted in human milk. No negative effects on breast-fed newborn/infant are anticipated. Fluarix may be given during lactation.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility in females.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed with Fluarix. Some of the effects mentioned under Adverse Reactions (e.g. fatigue or dizziness) may temporarily have minor influence on the ability to drive and use machines.

4.8 Undesirable effects

The safety profile for the currently licensed Fluarix was inferred from the previously licensed Fluarix.

Summary of the safety profile

For adults, most of solicited reactions usually occurred within the first 2 days following vaccination, lasted 3 days, and were mostly reported as mild to moderate in intensity.

For children from 6 months to 17 years of age, most of solicited reactions usually occurred on the day of vaccination, lasted 2 days, and were mostly reported as mild to moderate in intensity.

In all age groups the most frequently reported local adverse reaction after vaccination was injection site pain (21.5 % to 52.7 %).

In adults 18 years of age and older, the most frequently reported general adverse reactions after vaccination were fatigue (12.2 % to 31.4 %), headache (9.0 % to 21.9 %), and myalgia (12.2 % to 14.3 %).

In subjects aged 6 to less than 18 years, the most frequently reported general adverse reactions after vaccination were fatigue (10.5 % to 16.7 %), myalgia (10.7 % to 24.6 %), and headache (9.3 % to 14.4 %).

In subjects aged 3 to less than 6 years, the most frequently reported general adverse reactions after vaccination were drowsiness (7.3 % to 14.8 %), loss of appetite (5.5 % to 8.7 %), and irritability/fussiness (8.1 % to 15.4 %).

In subjects aged 6 to less than 36 months, the most frequently reported general adverse reactions after vaccination were irritability/fussiness (19 % to 30.1 %), drowsiness (13.5 % to 19.8 %), and loss of appetite (7.5 % to 18 %).

Tabulated list of adverse reactions

Adverse reactions reported are listed according to the following frequency categories:

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)

Clinical trial data

In controlled clinical studies, Fluarix was administered to more than 24 500 subjects aged 18 years and above and to more than 8 600 subjects from 6 months to less than 18 years of age.

The following adverse reactions per dose have been reported:

System Organ Class	**Adverse Reactions**	**Frequency**			
		6 to < 36 months	**3 to < 6 years**	**6 to < 18 years**	**≥ 18 years**
Metabolism and nutrition disorders	Loss of appetite	Very common	Very common	N/A	N/R
Psychiatric disorders	Irritability	Very common	Very common	N/A	N/R
Nervous system disorders	Headache	N/A	N/A	Very common	Very common
	Drowsiness	Very common	Very common	N/A	N/R
	Dizziness	N/R	N/R	N/R	Uncommon
Gastrointestinal disorders	Gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain)	Common	Common	Common	Common
Skin and subcutaneous tissue disorders	Sweating	N/R	N/R	N/R	Common
Musculoskeletal and connective tissue disorders	Myalgia	N/A	N/A	Very common	Very common
	Arthralgia	N/A	N/A	Common	Common

General disorders and administration site conditions	Fatigue	N/A	N/A	Very common	Very common
	Shivering	N/A	N/A	Common	Common
	Fever	Common	Common	Common	Uncommon
	Pain at the injection site	Very common	Very common	Very common	Very common
	Redness at the injection site	Very common	Very common	Very common	Common
	Swelling at the injection site	Very common	Very common	Very common	Common
	Induration at the injection site	N/R	N/R	N/R	Common

N/A=Not solicited in this age group
N/R=Not reported

Post-marketing data

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Rare	Transient lymphadenopathy
Immune system disorders	Rare	Allergic reactions (including anaphylactic reactions)
Nervous system disorders	Rare	Neuritis, acute disseminated encephalomyelitis, Guillain-Barré syndrome*
Skin and subcutaneous tissue disorders	Rare	Urticaria, pruritus, erythema, rash, angioedema
General disorders and administration site conditions	Rare	Influenza-like illness, malaise

*Spontaneous reports of Guillain-Barré syndrome have been received following vaccination with Fluarix; however, a causal association between vaccination and Guillain-Barré syndrome has not been established.

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/.
Additionally, you should also report to GSK Israel (il.safety@gsk.com).

4.9 Overdose

Insufficient data are available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC Code: J07BB02

Mechanism of action

Fluarix provides active immunisation against three influenza virus strains contained in the vaccine.

Fluarix induces humoral antibodies against the haemagglutinins. These antibodies neutralise influenza viruses.

Specific levels of haemagglutination-inhibition (HI) antibody titre post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HI antibody titres have been used as a measure of vaccine activity. In some human challenge trials, HI antibody titres of ≥ 1:40 have been associated with protection from influenza illness in up to 50 % of subjects.

Annual revaccination is advised because immunity declines during the year after vaccination, and because circulating strains of influenza virus might change from year to year.

Pharmacodynamic effects

Immunological data and estimates of efficacy of Fluarix have been evaluated in studies conducted either with Fluarix or with Fluarix Tetra.

Vaccine efficacy

Efficacy in children 6 to 35 months of age

The efficacy of Fluarix Tetra was evaluated in clinical study D-QIV-004, a randomised, observer-blind, non-influenza vaccine-controlled trial conducted during influenza seasons 2011 to 2014. Healthy subjects aged 6 through 35 months were randomized (1:1) to receive Fluarix Tetra (N=6 006) or a non-influenza control vaccine (N=6 012). They were administered 1 dose (in case of history of influenza vaccination) or 2 doses, approximately 28 days apart.

Efficacy of Fluarix Tetra was assessed for the prevention of reverse transcription polymerase chain reaction (RT-PCR)-confirmed influenza A and/or B disease (moderate to severe and of any severity) due to any seasonal influenza strain. Starting 2 weeks post-vaccination until the end of the influenza season (approximately 6 months later), nasal swabs were collected following an influenza like event, and tested for influenza A and/or B by RT-PCR. All RT-PCR-positive specimens were further tested for viability in cell culture and to determine whether the viral strains matched those in the vaccine.

Fluarix Tetra met the predefined criteria for primary and secondary Vaccine Efficacy objectives presented in Table 1.

Table 1: Fluarix Tetra: Attack Rates and Vaccine Efficacy in children 6-35 months of age (ATP (according to protocol) cohort for efficacy-time to event)

	Fluarix Tetra		Active comparator[1]		Vaccine Efficacy	
	N[2]=5 707		N[2]=5 697			
	n[3]	Attack Rate (n/N) (%)	n[3]	Attack Rate (n/N) (%)	%	CI
Any severity Influenza[6]						
RT-PCR confirmed	344	6.03	662	11.62	49.8	41.8; 56.8[4]
Culture confirmed	303	5.31	602	10.57	51.2	44.1; 57.6[5]
Culture confirmed vaccine matching strains	88	1.54	216	3.79	60.1	49.1; 69.0[5]
Moderate to Severe Influenza[7]						
RT-PCR confirmed	90	1.58	242	4.25	63.2	51.8; 72.3[4]
Culture confirmed	79	1.38	216	3.79	63.8	53.4; 72.2[5]
Culture confirmed vaccine matching strains	20	0.35	88	1.54	77.6	64.3; 86.6[5]
Lower respiratory Illness RT-PCR Confirmed	28	0.49	61	1.07	54.0	28.9; 71.0[5]
Acute Otitis media RT PCR-confirmed	12	0.21	28	0.49	56.6	16.7; 78.8[5]

CI: Confidence Interval

[1]Children received age-appropriate non-influenza vaccine control

[2]Number of subjects included in the ATP cohort for efficacy-time to event. This cohort included subjects who met all eligibility criteria, who were followed for efficacy and complied with the study protocol until the episode.

[3]Number of subjects who reported at least one case in the reporting period

[4]Two-sided 97.5 % confidence interval

[5]Two-sided 95 % confidence interval

[6]Influenza disease of any severity was defined as an episode of influenza-like illness (ILI, i.e. fever ≥ 38 °C with any of the following: cough, runny nose, nasal congestion, or breathing difficulty) or a consequence of influenza virus infection [acute otitis media (AOM) or lower respiratory illness (LRI)].

[7]Moderate to severe influenza was a subset of any influenza disease, with any of the following: fever > 39 °C, physician-diagnosed AOM, physician-diagnosed lower respiratory tract infection, physician-diagnosed serious extra-pulmonary complications, hospitalisation in the intensive care unit, or supplemental oxygen required for more than 8 hours.

Exploratory analyses were conducted on the Total Vaccinated Cohort including 12 018 subjects (N=6 006 for Fluarix Tetra, N=6 012 for control). Fluarix Tetra was efficacious in the prevention of moderate to severe influenza caused by each of the 4 strains (Table 2), even when there was significant antigenic mismatch with 2 of the vaccine strains (A/H3N2 and B/Victoria).

Table 2: Fluarix Tetra: Attack Rates and Vaccine Efficacy for RT-PCR confirmed moderate to severe disease by Influenza A subtypes and Influenza B lineages in children 6-35 months of age (Total Vaccinated Cohort)

	Fluarix Tetra		Active comparator[1]		Vaccine Efficacy	
	N[2]=6 006		N[2]=6 012			
Strain	n[3]	Attack Rate (n/N) (%)	n[3]	Attack Rate (n/N) (%)	%	95 % CI
A						
H1N1[4]	13	0.22	46	0.77	72.1	49.9; 85.5
H3N2[5]	53	0.88	112	1.86	52.7	34.8; 66.1
B						
Victoria[6]	3	0.05	15	0.25	80.1	39.7; 95.4

Yamagata[7]	22	0.37	73	1.21	70.1	52.7; 81.9

CI: Confidence Interval
[1]Infants received age-appropriate non-influenza vaccine control
[2]Number of subjects included in the Total Vaccinated cohort
[3]Number of subjects who reported at least one case in the reporting period
[4 to 7]Proportion of antigenic matching strains was 84.8 %, 2.6 %, 14.3 % and 66.6 %, for A/H1N1, A/H3N2, B/Victoria, and B/Yamagata, respectively.

Additionally, for RT-PCR confirmed cases of any severity, Fluarix Tetra reduced the risk of visits to the general practitioner by 47 % (Relative Risk (RR): 0.53 [95 % CI: 0.46; 0.61], i.e., 310 versus 583 visits) and to the emergency room by 79 % (RR: 0.21 [95 % CI: 0.09; 0.47], i.e., 7 versus 33 visits). The use of antibiotics was reduced by 50 % (RR: 0.50 [95 % CI: 0.42; 0.60], i.e., 172 versus 341 subjects).

Efficacy in adults 18 years of age and older

The efficacy of Fluarix was evaluated in clinical study Fluarix-US-006, a randomised, double-blind, placebo-controlled study. The study evaluated efficacy in 7 652 subjects (N=5 103 for Fluarix and N=2 549 for Placebo) to prevent culture-confirmed influenza A and/or B cases for vaccine antigenically matched strains.

Subjects were monitored for influenza-like illnesses followed by culture-confirmed influenza (Table 3). Influenza-like illness was defined as at least one general symptom (fever ≥ 37.8 °C and/or myalgia) and at least one respiratory symptom (cough and/or sore throat).

Table 3: Attack Rates and Vaccine Efficacy against Illness associated with evidence of influenza A or B Infection in adults 18 to 64 years of age (Total Vaccinated Cohort)

	Fluarix		**Placebo**		**Vaccine Efficacy**	
	N[1]=5 103		**N[1]=2 549**			
	n[2]	**Attack Rate (n/N) (%)**	**n[2]**	**Attack Rate (n/N) (%)**	**%**	**95 % CI**
Antigenically matched, culture-confirmed Influenza[3]	49	1.0	74	2.9	66.9	51.9; 77.4
All culture-confirmed Influenza (Matched, Unmatched and Untyped)[4]	63	1.2	82	3.2	61.6	46.0; 72.8

CI: Confidence Interval
[1]total number of subjects
[2]number of cases
[3]There were no vaccine matched culture-confirmed cases of A/New Caledonia/20/1999 (H1N1) or B/Malaysia/2506/2004 influenza strains with Fluarix or placebo
[4]Of the 22 additional cases, 18 were unmatched and 4 were untyped; 15 of the 22 cases were A (H3N2) (11 cases with Fluarix and 4 cases with placebo)

Immunogenicity data

Immunogenicity of Fluarix Tetra was evaluated in terms of HI Geometric mean antibody titre (GMT) and HI seroconversion rate (4-fold rise in reciprocal titre or change from undetectable [< 10] to a reciprocal titre of ≥ 40) at Day 28 (children) or at Day 21 (adults) after the last dose.

Immunogenicity in children 6 to 35 months of age

In study D-QIV-004, the evaluation was performed in a sub-cohort of 1 332 children (753 in the Fluarix Tetra group and 579 in the control group). The results are presented in Table 4.

Table 4: Post-vaccination GMT and seroconversion rates in children (6-35 months) (According to Protocol Cohort)

	Fluarix Tetra		Control[3]	
	N[1]=750-753	N[2]=742-746	N[1]=578-579	N[2]=566-568
	GMT[4] (95 % CI)	Seroconversion rate[2] (95 % CI)	GMT[4] (95 % CI)	Seroconversion rate[4] (95 % CI)
A/H1N1	165.3 (148.6; 183.8)	80.2 % (77.2; 83.0)	12.6 (11.1; 14.3)	3.5 % (2.2; 5.4)
A/H3N2	132.1 (119.1; 146.5)	68.8 % (65.3; 72.1)	14.7 (12.9; 16.7)	4.2 % (2.7; 6.2)
B (Victoria)	92.6 (82.3; 104.1)	69.3 % (65.8; 72.6)	9.2 (8.4; 10.1)	0.9 % (0.3; 2.0)
B (Yamagata)	121.4 (110.1; 133.8)	81.2 % (78.2; 84.0)	7.6 (7.0; 8.3)	2.3 % (1.2; 3.9)

CI: Confidence Interval
[1]Number of subjects with post-vaccination results available (for GMT)
[2]Number of subjects with both pre- and post-vaccination results available (for SCR)
[3]non-influenza vaccine control
[4]results from the immunogenicity subcohort

The effect of a 2-dose priming schedule in D-QIV-004 was evaluated by assessing the immune response after revaccination one year later with 1 dose of Fluarix Tetra in study D-QIV-009. This study demonstrated that 7 days post-vaccination, immune memory in children 6 to 35 months of age had been elicited for all four vaccine strains.

Immunogenicity in children 3 to less than 18 years of age

In a phase III, double-blind study (D-QIV-003), children were randomised to receive 1 or 2 doses (depending on history of influenza vaccination) of either Fluarix (N=818) or Fluarix Tetra (N=791). The immune responses elicited by Fluarix and Fluarix Tetra are presented in Table 5.

Table 5: Post-vaccination GMT and seroconversion rates in children (3 to < 18 years) (According to Protocol Cohort)

	Fluarix[3]		Fluarix Tetra	
	N[1]=818	N[2]=818	N[1]=791	N[2]=790
	GMT (95 % CI)	Seroconversion rate (95 % CI)	GMT (95 % CI)	Seroconversion rate (95 % CI)
A/H1N1	433.2 (401.0; 468.0)	89.9 % (87.6; 91.8)	386.2 (357.3; 417.4)	91.4 % (89.2; 93.3)
A/H3N2	227.3 (213.3; 242.3)	70.7 % (67.4; 73.8)	228.8 (215.0; 243.4)	72.3 % (69.0; 75.4)
B (Victoria)	245.6 (229.2; 263.2)	68.5 % (65.2; 71.6)	244.2 (227.5; 262.1)	70.0 % (66.7; 73.2)
B (Yamagata)	224.7 (207.9; 242.9)	37.0 % (33.7; 40.5)	569.6 (533.6; 608.1)	72.5 % (69.3; 75.6)

CI: Confidence Interval
[1]Number of subjects with post-vaccination results available (for GMT)
[2]Number of subjects with both pre- and post-vaccination results available (for SCR)
[3]B (Yamagata) strain was not included in Fluarix

Immunogenicity in adults 18 years of age and older

In a phase III, randomised, partially blind study (D-QIV-008), approximately 600 subjects received 1 dose of Fluarix and approximately 1 800 subjects received 1 dose of Fluarix Tetra. The immune responses elicited by Fluarix and Fluarix Tetra are presented in Table 6.

Table 6: Post-vaccination GMT and seroconversion rates in adults 18 years or older (According to Protocol Cohort)

	Fluarix[3]		**Fluarix Tetra**	
	N[1]=608	**N[2]=605**	**N[1]=1 809**	**N[2]=1 801**
	GMT (95 % CI)	**Seroconversion rate (95 % CI)**	**GMT (95 % CI)**	**Seroconversion rate (95 % CI)**
A/H1N1	218.4 (194.2; 245.6)	77.2 % (73.6; 80.5)	201.1 (188.1; 215.1)	77.5 % (75.5; 79.4)
A/H3N2	298.2 (268.4; 331.3)	65.8 % (61.9; 69.6)	314.7 (296.8; 333.6)	71.5 % (69.3; 73.5)
B (Victoria)	393.8 (362.7; 427.6)	55.4 % (51.3; 59.4)	404.6 (386.6; 423.4)	58.1 % (55.8; 60.4)
B (Yamagata)	386.6 (351.5; 425.3)	45.6 % (41.6; 49.7)	601.8 (573.3; 631.6)	61.7 % (59.5; 64.0)

CI: Confidence Interval
[1]Number of subjects with post-vaccination results available (for GMT)
[2]Number of subjects with both pre- and post-vaccination results available (for SCR)
[3]B(Yamagata) strain was not included in Fluarix

Concomitant administration

Concomitant administration with pneumococcal vaccines

In clinical study D-QIV-010 involving 356 adults ≥ 50 years of age at risk for complications of influenza and pneumococcal diseases, subjects received Fluarix Tetra and 23-valent pneumococcal polysaccharide vaccine (PPV23) either concomitantly or non-concomitantly. For all four Fluarix Tetra vaccine strains and the six pneumococcal serotypes (1, 3, 4, 7F, 14, and 19A) in PPV23 evaluated in the pre-specified primary analysis, the immune response was non-inferior between the two treatment groups.

Immunological non-inferiority has been demonstrated based on published data for all 3 Fluarix strains and all 13-valent pneumococcal conjugate vaccine (PCV13) serotypes in adults 50-59 years of age, as well as for 2 of 3 Fluarix strains and 12 of 13 PCV13 serotypes in adults > 65 years of age. A lower immune response to some pneumococcal serotypes was observed when PCV13 was given concomitantly with Fluarix as compared to non-concomitant administration, however the clinical relevance of this observation is unknown.

Concomitant administration with adjuvanted herpes zoster vaccine (Shingrix)

In clinical study Zoster-004, 828 adults ≥ 50 years of age were randomised to receive 2 doses of Shingrix 2 months apart, administered either concomitantly at the first dose (N=413) or non-concomitantly (N=415) with one dose of Fluarix Tetra. Immunological non-inferiority between concomitant and non-concomitant administration was demonstrated for all four strains included in Fluarix Tetra in terms of HI antibody GMTs.

Concomitant administration with COVID-19 mRNA vaccine

In clinical study Zoster-091, 988 adults ≥ 18 years of age received Fluarix Tetra and monovalent COVID-19 mRNA-1273 booster (50 micrograms) vaccine (original SARS-CoV-2 strain) either concomitantly (N=498) or non-concomitantly, administered two weeks apart (N=490). Immunological non-inferiority between concomitant and non-concomitant administration was demonstrated for all four strains included in Fluarix Tetra in terms of HI antibody GMTs, and for the COVID-19 mRNA-1273 booster vaccine in terms of anti-S protein antibody GMC.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on general safety studies.

Reproductive and developmental study with Fluarix did not reveal vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Disodium hydrogen phosphate dodecahydrate
Polysorbate 80
Potassium dihydrogen phosphate
RRR- α-tocopheryl hydrogen succinate
Potassium chloride
Octoxinol 10
Magnesium chloride hexahydrate
Water for injections

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.

Store in the original package in order to protect from light.

Stability data indicate that Fluarix remains stable at temperatures up to 25 °C for 72 hours. If not used at the end of this period, the vaccine should be discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.5 Nature and contents of container

0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.

The tip cap and rubber plunger stopper of the pre-filled syringe are made with synthetic rubber.

Pack sizes of 1 and 10, with or without needles.

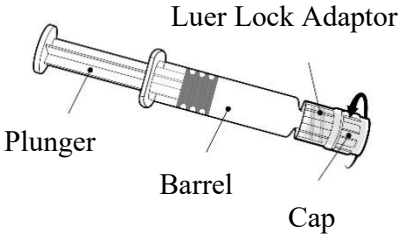
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Vaccines should be inspected visually for any foreign particulate matter and/or variation of physical aspects prior to administration. Before use, the vaccine should be well shaken to obtain a colourless and slightly opalescent liquid. Discard if the content appears otherwise.

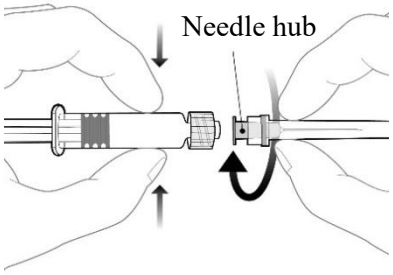
The entire content of the syringe should be injected.

Instructions for the pre-filled syringe



Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.



To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

Disposal

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

7. MANUFACTURER

GlaxoSmithKline Biologicals S.A., Rixensart, Belgium

8. LICENSE HOLDER

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva

9. LICENSE NUMBER

179-96-38199-00

Approved on August 2025

Fluarix DR V1