For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

FLUARIX TETRA
2024 South

1. GENERIC NAME

Inactivated Influenza Vaccine (Split Virion) IP

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/Thailand/8/2022 (H3N2)-like strain (A/Thailand/8/2022, IVR- 237)	15 micrograms HA**
B/Austria/1359417/2021 - like strain (B/Austria/1359417/2021, BVR-26)	15 micrograms HA**
B/Phuket/3073/2013 - like strain (B/Phuket/3073/2013, wild type)	15 micrograms HA**

per 0.5 ml dose

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

This vaccine complies with the World Health Organisation (WHO) recommendation (Southern Hemisphere) for the 2024 season.

FLUARIX TETRA may contain traces of eggs (such as ovalbumin, chicken proteins), formaldehyde, gentamicin sulphate and sodium deoxycholate which are used during the manufacturing process (see *section 4.3 Contraindications*).

List of excipients
Sodium chloride,
Disodium phosphate dodecahydrate,
Potassium dihydrogen phosphate,
Potassium chloride,
Magnesium chloride hexahydrate,
α-tocopheryl hydrogen succinate,
Polysorbate 80,
Octoxinol 10
Water for injections.

3. DOSAGE FORM AND STRENGTH

Suspension for injection in a pre-filled syringe.

The suspension is colourless and slightly opalescent.

For strength, see section 2 Qualitative and Quantitative Composition

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

FLUARIX TETRA 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 the two influenza B virus types contained in the vaccine.

4.2 Posology and Method of Administration

Posology

Adults: 0.5 ml.

Pediatric Population:

Children from 6 months onwards: 0.5 ml.

For children aged < 9 years, who have not previously been vaccinated against influenza, a second dose should be given after an interval of at least 4 weeks.

Children less than 6 months: the safety and efficacy of *FLUARIX TETRA* in children less than 6 months have not been established.

Method of Administration

Immunisation should be carried out by intramuscular injection.

Precautions to be taken before handling or administering the medicinal product.

For instructions for preparation of the medicinal product before administration, see *section 8.4 Storage and Handling Instructions*

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in *section 2 List of excipients* or to any component that may be present as traces such as eggs (ovalbumin, chicken proteins), formaldehyde, gentamicin sulphate and sodium deoxycholate.

Immunisation shall be postponed in patients with febrile illness or acute infection.

4.4 Special Warnings and Precautions for Use

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.

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

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

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

FLUARIX TETRA should under no circumstances be administered intravascularly.

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

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.

Interference with serological testing, see *section 4.5 Drug Interactions.*

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

This medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially ‘potassium-free’.

4.5 Drug Interactions

FLUARIX TETRA can be concomitantly administered with pneumococcal polysaccharide vaccines in subjects aged 50 years and above (see *section 5.2 Pharmacodynamic Properties*).

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

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

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 observed. The Western Blot technique disproves the false-positive ELISA test results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6 Use in Special Populations

Pregnancy

Inactivated influenza vaccines 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; however, data from worldwide use of inactivated influenza vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

Breast-feeding

FLUARIX TETRA may be used during breast-feeding.

Fertility

No fertility data are available.

4.7 Effects on Ability to Drive and Use Machines

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

4.8 Undesirable Effects

Clinical trials

Summary of the safety profile

In all age groups, the most frequently reported local adverse reaction after vaccination was injection site pain (15.6% to 40.9%).

In adults 18 years of age and above, the most frequently reported general adverse reactions after vaccination were fatigue (11.1%), headache (9.2%) and myalgia (11.8%).

In subjects aged 6 to 17 years, the most frequently reported general adverse reactions after vaccination were fatigue (12.6%), myalgia (10.9%) and headache (8.0%).

In subjects aged 3 to 5 years, the most frequently reported general adverse reactions after vaccination were drowsiness (9.8%) and irritability (11.3%).

In subjects aged 6 months to 3 years, the most frequently reported general adverse reactions after vaccination were irritability/fussiness (14.9%) and loss of appetite (12.9%).

Tabulated list of adverse reactions

Adverse reactions reported for *FLUARIX TETRA* in the different age groups are listed per dose 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)

Adults

A clinical study with *FLUARIX TETRA* in adults has evaluated the incidence of adverse reactions in subjects ≥18 years who received one dose of *FLUARIX TETRA* (N = 3036) or *FLUARIX* (trivalent influenza vaccine) (N = 1010).

The following adverse reactions per dose have been reported:

System Organ Class	Frequency	Adverse Reactions
Nervous system disorders	Common	Headache
	Uncommon	Dizziness[1]
Gastrointestinal disorders	Common	Gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain)
Skin and subcutaneous tissue disorders	Common	Sweating[2]
Musculoskeletal and connective tissue disorders	Very common	Myalgia
	Common	Arthralgia
General disorders and administration site conditions	Very common	Injection site pain, fatigue
	Common	Injection site redness, injection site swelling, shivering, fever, injection site induration[2]
	Uncommon	Injection site haematoma[1], injection site pruritus[1]

[1]Reported as unsolicited adverse reaction
[2]Reported in previous *FLUARIX* trials

Children aged 6 months to <18 years

Two clinical studies evaluated the reactogenicity and safety of *FLUARIX TETRA* in children who received at least one dose of *FLUARIX TETRA* or a control vaccine.

One study enrolled children 3 to <18 years of age who received *FLUARIX TETRA* (N = 915) or *FLUARIX* (N = 912). The second study enrolled children 6 to <36 months of age who received *FLUARIX TETRA* (N = 6006) or a non-influenza vaccine control (N = 6012) (see *section 5.2 Pharmacodynamic properties*).

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)
Metabolism and nutrition disorders	Loss of appetite	Very common	Common	N/A
Psychiatric disorders	Irritability/Fussiness	Very common	Very common	N/A
Nervous system disorders	Drowsiness	Very common	Common	N/A
	Headache	N/A	N/A	Common
Gastrointestinal disorders	Gastrointestinal symptoms (including nausea, diarrhoea, vomiting and/or abdominal pain)	N/A	N/A	Common

Skin and subcutaneous tissue disorders	Rash[1]	N/R	Uncommon	Uncommon
Musculoskeletal and connective tissue disorders	Myalgia	N/A	N/A	Very common
	Arthralgia	N/A	N/A	Common
General disorders and administration site conditions	Fever (≥38.0°C)	Common	Common	Common
	Fatigue	N/A	N/A	Very common
	Injection site pain	Very common	Very common	Very common
	Injection site redness	Very common	Very common	Very common
	Injection site swelling	Common	Very common	Very common
	Shivering	N/A	N/A	Common
	Injection site pruritus[1]	N/R	Uncommon	Uncommon
	Injection site induration[2]	N/A	Common	Common

N/A=Not solicited in this age group
N/R=Not reported
[1]Reported as unsolicited adverse reaction
[2]Reported in previous *FLUARIX* trials

Post-marketing data

The following adverse reactions have been observed for *FLUARIX* and/or *FLUARIX TETRA* during post-marketing surveillance[1].

System Organ Class	Frequency	Adverse events
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[2]
Skin and subcutaneous tissue disorders	Rare	Urticaria, pruritus, erythema, angioedema
General disorders and administration site conditions	Rare	Influenza-like illness, malaise

[1]Three of the influenza strains contained in *FLUARIX* are included in *FLUARIX TETRA*.
[2]Spontaneous reports of Guillain-Barré syndrome have been received following vaccination with *FLUARIX* and *FLUARIX TETRA*; however, a causal association between vaccination and Guillain-Barré syndrome has not been established.

4.9 **Overdose**

Overdosage is unlikely to have any untoward effect.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

FLUARIX TETRA provides active immunisation against four influenza virus strains (two A subtypes and two B lineages) contained in the vaccine.

FLUARIX TETRA 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 studies, HI antibody titres of ≥ 1:40 have been associated with protection from influenza illness in up to 50% of subjects.

5.2 Pharmacodynamic Properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02.

Pharmacodynamic effects

Efficacy in children 6-35 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]	**n[3]**	**Attack rate (n/N) (%)**	**N[2]**	**n[3]**	**Attack rate (n/N) (%)**	**%**	**CI**
Any severity Influenza[6]								
RT-PCR confirmed	5,707	344	6.03	5,697	662	11.62	49.8	41.8; 56.8[4]
Culture confirmed	5,707	303	5.31	5,697	602	10.57	51.2	44.1; 57.6[5]
Culture confirmed vaccine matching strains	5,707	88	1.54	5,697	216	3.79	60.1	49.1; 69.0[5]
Moderate to Severe Influenza[7]								
RT-PCR confirmed	5,707	90	1.58	5,697	242	4.25	63.2	51.8; 72.3[4]
Culture confirmed	5,707	79	1.38	5,697	216	3.79	63.8	53.4; 72.2[5]
Culture confirmed vaccine matching strains	5,707	20	0.35	5,697	88	1.54	77.6	64.3; 86.6[5]
Lower respiratory Illness RT-PCR Confirmed	5,707	28	0.49	5,697	61	1.07	54.0	28.9; 71.0[5]
Acute Otitis media RT PCR-confirmed	5,707	12	0.21	5,697	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]2-sided 97.5% confidence interval

[5]2-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 12018 subjects (N = 6006 for *FLUARIX TETRA*, N = 6012 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**	
Strain	**N[2]**	**n[3]**	**Attack rate (n/N) (%)**	**N[2]**	**n[3]**	**Attack rate (n/N) (%)**	**%**	**95% CI**
A								
H1N1[4]	6006	13	0.22	6012	46	0.77	72.1	49.9; 85.5
H3N2[5]	6006	53	0.88	6012	112	1.86	52.7	34.8; 66.1
B								
Victoria[6]	6006	3	0.05	6012	15	0.25	80.1	39.7; 95.4
Yamagata[7]	6006	22	0.37	6012	73	1.21	70.1	52.7; 81.9

[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 18-64 years of age

A clinical study performed in more than 7,600 subjects in the Czech Republic and Finland evaluated the efficacy of *FLUARIX* to prevent culture-confirmed influenza A and/or B cases for vaccine antigenically matched strains.

Subjects were monitored for influenza-like illness to be confirmed by culture (see table 3 for results). 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)

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

[1]n/N: number of case/total number of subjects
[2]CI: Confidence Interval
[3]LL: Lower Limit
[4]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.
[5]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).

In this study, immunogenicity was also evaluated.

Table 4: Post-vaccination GMT and seroconversion rates

Adults 18 years to 64 years	*FLUARIX*[1] N=291
	GMT (95% CI)
A/H1N1	541.0 (451.0;649.0)
A/H3N2	133.2 (114.6;154.7)
B (Victoria)	242.8 (210.7;279.7)
	Seroconversion rate (95% CI)
A/H1N1	76.3% (71.0;81.1)
A/H3N2	73.9% (68.4;78.8)
B (Victoria)	85.2% (80.6;89.1)

[1]containing A/H1N1, A/H3N2 and B (Victoria lineage)

Post-vaccination seroprotection rates were 97.6% against A/H1N1, 86.9% against A/H3N2 and 96.2% against B (Victoria).

Immunogenicity in children and adults:

Immunogenicity of *FLUARIX TETRA* was evaluated in terms of HI Geometric mean antibody titre (GMT) at 28 days after the last dose (children) or Day 21 (adults) and HI

seroconversion rate (4-fold rise in reciprocal titre or change from undetectable [< 10] to a reciprocal titre of ≥ 40).

In study D-QIV-004 (children 6-35 months), 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 5.

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.

Immunogenic non-inferiority of *FLUARIX TETRA* was assessed versus *FLUARIX* in children in study D-QIV-003 (approximately 900 children 3 to < 18 years of age in each treatment group who received one or two doses of either vaccine) and adults in study D-QIV-008 (approximately 1,800 subjects 18 years of age and older received 1 dose of *FLUARIX TETRA* and approximately 600 subjects received 1 dose of *FLUARIX*). In both studies, *FLUARIX TETRA* elicited an immune response against the three strains in common that was non-inferior to *FLUARIX* and a superior immune response against the additional B strain included in *FLUARIX TETRA*. The results are presented in Table 5.

Table 5: *FLUARIXTETRA*: Post-vaccination GMT and seroconversion rates (SCR) in children (6-35 months; 3 to < 18 years) and adults 18 years or older (According to Protocol Cohort)

Children 6 to 35 months of age (D-QIV-004)				
	FLUARIX TETRA		**Control[1]**	
	N=750-753	**N'=742-746**	**N=578-579**	**N'=566-568**
	GMT[2] (95% CI)	**Seroconversion rate[2] (95% CI)**	**GMT[2] (95% CI)**	**Seroconversion rate[2] (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)
Children 3 to < 18 years (D-QIV-003)				
	FLUARIX TETRA		***FLUARIX*[3]**	
	N=791	**N'=790**	**N=818**	**N'=818**
	GMT (95% CI)	**Seroconversion rate (95% CI)**	**GMT (95% CI)**	**Seroconversion rate (95% CI)**
A/H1N1	386.2 (357.3;417.4)	91.4% (89.2;93.3)	433.2 (401.0;468.0)	89.9% (87.6;91.8)
A/H3N2	228.8 (215.0;243.4)	72.3% (69.0;75.4)	227.3 (213.3;242.3)	70.7% (67.4;73.8)
B (Victoria)	244.2 (227.5;262.1)	70.0% (66.7;73.2)	245.6 (229.2;263.2)	68.5% (65.2;71.6)
B (Yamagata)	569.6 (533.6;608.1)	72.5% (69.3;75.6)	224.7 (207.9;242.9)	37.0% (33.7;40.5)
Adults 18 years or older (D-QIV-008)				
	FLUARIX TETRA		***FLUARIX*[3]**	
	N=1,809	**N'=1,801**	**N=608**	**N'=605**
	GMT (95% CI)	**Seroconversion rate (95% CI)**	**GMT (95% CI)**	**Seroconversion rate (95% CI)**
A/H1N1	201.1 (188.1;215.1)	77.5% (75.5;79.4)	218.4 (194.2;245.6)	77.2% (73.6;80.5)
A/H3N2	314.7 (296.8;333.6)	71.5% (69.3;73.5)	298.2 (268.4;331.3)	65.8% (61.9;69.6)
B (Victoria)	404.6 (386.6;423.4)	58.1% (55.8;60.4)	393.8 (362.7;427.6)	55.4% (51.3;59.4)
B (Yamagata)	601.8 (573.3;631.6)	61.7% (59.5;64.0)	386.6 (351.5;425.3)	45.6% (41.6;49.7)

N = Number of subjects with post-vaccination results available (for GMT)

N' = Number of subjects with both pre- and post-vaccination results available (for SCR)

[1]non-influenza vaccine control

[2]results from the immunogenicity subcohort

[3] B (Yamagata) strain was not included in *FLUARIX.*

Concomitant administration with pneumococcal polysaccharide 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 separately. 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. Based on a descriptive analysis for six additional pneumococcal vaccine serotypes (5, 6B, 9V, 18C, 19F, and 23F), the immune response was comparable between groups, with 91.7% to 100% and 90.7% to 100% of subjects attaining seroprotective antibody levels against these serotypes in the separate and concomitant administration group respectively.

5.3 Pharmacokinetic properties

Not Applicable.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Non-clinical data reveal no special hazards for humans based on conventional studies of acute toxicity, local tolerance, repeated dose toxicity and reproductive/developmental toxicity.

7. DESCRIPTION

FLUARIXTETRA is a sterile, colourless and slightly opalescent liquid suspension of purified split inactivated influenza virus, presented in glass (Type I) syringes, each syringe containing a single 0.5-mL dose, intended for intramuscular injection. The vaccine is preservative-free.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

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

8.2 Shelf life

12 months.

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

0.5 ml suspension in prefilled syringe (Type I glass) with a plunger stopper (grey butyl rubber) and a tip cap (bromobutyl and synthetic polyisoprene type I rubber) with or without needles in the following pack sizes:

- with 1 needle: pack sizes of 1 or 10
- with 2 needles: pack size of 1
- without needle: pack sizes of 1 or 10

All packs may not be marketed in India.

8.4 Storage and Handling Instructions

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

Do not freeze.

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

Keep out of reach of children.

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

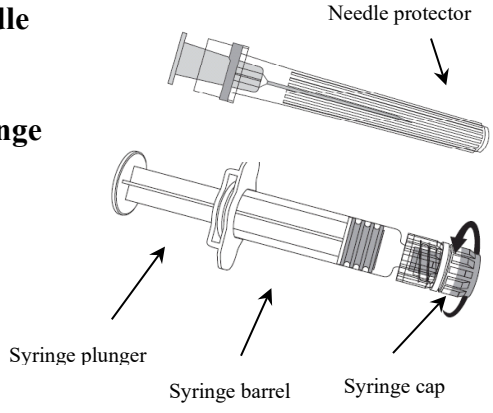
Shake well before use. Inspect visually prior to administration.

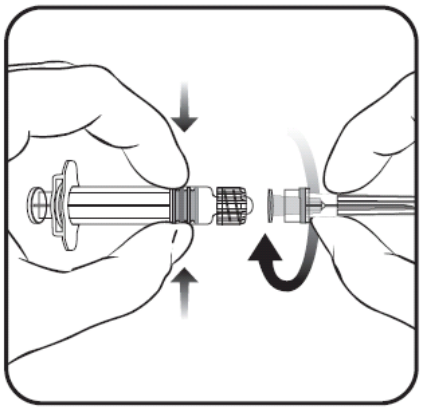
<u>Instructions for administration of the vaccine presented in pre-filled syringe.</u>

To attach the needle to the syringe, refer to the below drawing.

Needle

Syringe





1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock. (see picture)
3. Remove the needle protector, which on occasion can be a little stiff.
4. Administer the vaccine.

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

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) of the potential benefits and undesirable effects of vaccination with *FLUARIXTETRA*. Patients (and/or patients' caregiver) may also be informed about posology (including vaccination schedule if applicable), method of administration and storage/handling information of *FLUARIX TETRA* vaccine as applicable.

Registered Medical Practitioners may also choose to inform their patients (and/or patients' caregiver) about the special warnings and precautions for use, drug interactions, and any relevant contraindications associated with *FLUARIX TETRA* vaccine.

10. DETAILS OF MANUFACTURER

M/s. GlaxoSmithKline Biologicals, branch of SmithKline Beecham Pharma GmbH & Co. KG 40 Zirkusstraβe- D-01069 Dresden, Germany

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office
252, Dr Annie Besant Road,
Worli,
Mumbai 400030, India.

9. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Marketing Authorization Holder: M/s. GlaxoSmithKline Pharmaceuticals Limited, 252, Dr. Annie Besant Road, Worli, Mumbai 400 030, India.

Marketing Authorization Details:
Import Permission No.: IMP/BIO/19/000003 dated 04-Apr-2019

10. DATE OF REVISION

DD-MMM-YYYY

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Version FLXT-SH/PI/IN/2023/01 dated 26-Oct-2023.

Adapted from EMA SPC dated 04-Aug-2022 [GDS 05/IPI SH v18] and based on WHO recommended strains (Southern Hemisphere) for the season 2024.