AUSTRALIAN PRODUCT INFORMATION

FLUARIX TETRA (Influenza virus haemagglutinin) suspension for injection

1 NAME OF THE MEDICINE

Quadrivalent influenza vaccine (split virion, inactivated)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

FLUARIX TETRA is an inactivated and purified split influenza vaccine. The antigen composition and strains for the 2024 influenza season corresponds to the following types:

A/Victoria/4897/2022 (H1N1)pdm09-like strain

A/Thailand/8/2022 (H3N2)-like strain

B/Austria/1359417/2021-like strain

B/Phuket/3073/2013-like strain

FLUARIX TETRA is prepared using whole virus cultivated in embryonated hens' eggs. The virus is concentrated and purified by clarification, adsorption and centrifugation. The purified whole virus is then treated with the detergent sodium deoxycholate and again centrifuged, and the resulting antigen suspension is inactivated with formaldehyde.

Each 0.5 mL vaccine dose contains 15 micrograms haemagglutinin of each of four influenza strains in phosphate buffered saline.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

FLUARIX TETRA meets the WHO requirements for biological substances and influenza vaccines and the European Pharmacopoeia requirements for influenza vaccines.

The type and amount of viral antigens in FLUARIX TETRA conform to the annual requirements of the Australian Influenza Vaccine Committee (AIVC) and the New Zealand Ministry of Health.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Suspension for injection.

FLUARIX TETRA is a colourless to slightly opalescent suspension.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

FLUARIX TETRA is a quadrivalent vaccine indicated for active immunisation of adults and children from 6 months of age for the prevention of influenza disease caused by the influenza virus types A and B contained in the vaccine (see section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials).

The use of FLUARIX TETRA should be based on official recommendations.

4.2 DOSE AND METHOD OF ADMINISTRATION

FLUARIX TETRA should under no circumstances be administered intravascularly.

Children aged <6 months

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

Dosage

FLUARIX TETRA should be administered as a single 0.5 mL injection.

Children 6 months to less than 9 years of age who have not previously been vaccinated against influenza should receive a second dose of 0.5 mL after an interval of at least 4 weeks.

Administration

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

4.3 CONTRAINDICATIONS

FLUARIX TETRA should not be administered to individuals with known hypersensitivity after previous administration of FLUARIX TETRA or influenza vaccines or to any component of the vaccine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

FLUARIX TETRA should under no circumstances be administered intravascularly.

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.

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

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

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.

Patients with a history of Guillain-Barre Syndrome (GBS) with an onset within six weeks of an influenza vaccination may be at increased risk of again developing GBS if given influenza vaccine. Such risk should be weighed against the benefits to the individual patient of influenza vaccination.

As patients with a history of GBS have an increased likelihood of again developing the syndrome, the chance of them coincidently developing the syndrome following influenza vaccination may be higher than in individuals with no history of GBS.

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

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 individuals.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Latex

Prefilled syringe with attached needle

This presentation of FLUARIX TETRA cannot be considered latex-free. The removable needle shield contains natural rubber latex.

Prefilled syringe with separate needle

The syringe cap, syringe plunger and needle protector of the prefilled syringes of FLUARIX TETRA with separate needles are not made with natural rubber latex.

Use in the elderly

Antibody responses were lower in older adults who received FLUARIX TETRA than in younger subjects. In a randomised, double-blind (2 arms) and open-label (one arm), active-controlled study, immunogenicity and safety were evaluated in a cohort of subjects 65 years of age and older who received FLUARIX TETRA (N = 1,517); 469 of these subjects were 75 years of age and older. In subjects 65 years of age and older, the geometric mean antibody titers post-vaccination and seroconversion rates were lower than in younger subjects (18 through 64 years of age) and the frequencies of solicited and unsolicited adverse events were generally lower than in younger subjects.

Paediatric use

Refer to information above in section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Effects on laboratory tests

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).

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

FLUARIX TETRA can be concomitantly administered with adjuvanted herpes zoster vaccine (SHINGRIX) (see section 5.1 PHARMACODYNAMIC PROPERTIES).

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 similar to that observed with SHINGRIX alone, and higher compared to FLUARIX TETRA alone.

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.

Influenza vaccine can impair the metabolism of warfarin, theophylline, phenytoin, phenobarbitone and carbamazepine by the hepatic cytochrome P450 system. Results from studies have been variable in degree of interaction and time after vaccination for the interaction to take effect. The interaction may be variable from individual to individual. Patients taking warfarin, theophylline, phenytoin, phenobarbitone or carbamazepine should be advised of the possibility of an interaction and told to look out for signs of elevated levels of their medication.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

A reproductive and developmental toxicity study in which female rats were administered FLUARIX TETRA (0.2 mL dose per rat, approximately 80x the human dose on the basis of bodyweight) twice prior to mating showed no adverse effects on female fertility.

Use in pregnancy

(Pregnancy Category A)

A developmental and reproductive toxicity study has been performed in which female rats were administered FLUARIX TETRA by IM injection (0.2 mL dose per rat, approximately 80x the human dose on the basis of bodyweight) twice prior to mating, four times during gestation, and once on lactation day 7. Exposure to FLUARIX TETRA did not result in systemic maternal toxicity (no adverse clinical signs and no change in body weight or food consumption). In addition, no adverse effects on pregnancy, parturition, lactation, or embryo-foetal or pre-weaning development were observed. There were no vaccine-related foetal malformations or other evidence of teratogenesis noted in this study.

The Australian Department of Health has reviewed the considerable extent of immunisation of pregnant Australian women with inactivated influenza vaccines, the international published literature, the very limited reporting of possible adverse effects and the studies conducted by vaccine manufacturers and concluded that there is no increased risk of any adverse foetal or maternal outcomes attributable to the vaccine. FLUARIX TETRA can be given to a pregnant woman following an assessment of the risks and benefits. Because of the known adverse consequences of influenza infection in pregnant women, Australian health authorities recommend vaccination of pregnant women.

Use in lactation

The safety of FLUARIX TETRA when administered to breastfeeding women has not been evaluated. It is unknown whether FLUARIX TETRA is excreted in human breast milk.

Vaccine antigen-specific antibodies were transferred to rat pups via milk from dams administered FLUARIX TETRA during gestation and lactation, with no adverse effects.

FLUARIX TETRA should only be used during breast-feeding when the possible advantages outweigh the potential risks.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical trial data

Adverse reactions reported for FLUARIX TETRA in the different age groups 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

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 = 3,036) or FLUARIX (N = 1,010).

The following adverse reactions per dose have been reported:

Table 1: FLUARIX TETRA: Incidence of adverse reactions per dose in subjects ≥18 years of age

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 hematoma[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 = 6,006) or a non-influenza vaccine control (N = 6,012) (see section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials).

The following adverse reactions per dose have been reported:

Table 2: FLUARIX TETRA: Incidence of adverse reactions per dose in subjects aged 6 months to <18 years of age

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

The table below shows the incidence of solicited local and systemic adverse reactions overall/dose within 7 days[a] after vaccination in children aged 6 through 35 months[b] (Total Vaccinated Cohort):

Table 3: FLUARIX TETRA: Incidence of solicited local and systemic adverse reactions per dose within 7 days after vaccination in children aged 6 through 35 months (Total Vaccinated Cohort)

	FLUARIX TETRA %		**Non-Influenza Active Comparator[c,d] %**	
	Any	Grade 3[e]	Any	Grade 3[e]
Local	**n = 11,656**		**n = 11,662**	
Pain	15.6	0.4	16.0	0.4
Redness	11.7	0	12.5	0
Swelling	7.2	0	7.9	0
Systemic	**n = 11,653**		**n = 11,658**	
Irritability	14.9	0.7	15.5	1.0
Loss of appetite	12.9	1.0	13.3	0.9
Drowsiness	10.8	0.5	11.9	0.7
Fever[f]	6.1	1.2	6.8	1.3

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available. n = number of documented doses.

a Seven days included day of vaccination and the subsequent 6 days.

b Trial 7: NCT01439360 (FLU D-QIV-004).

c Children younger than 12 months: pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.).

d Children 12 months and older: HAVRIX (Hepatitis A Vaccine) for those with a history of influenza vaccination; or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) for those with no history of influenza vaccination.

e Grade 3 pain: Defined as cried when limb was moved/spontaneously painful.
Grade 3 swelling, redness: Defined as >50 mm.
Grade 3 irritability: Defined as crying that could not be comforted/prevented normal activity.
Grade 3 loss of appetite: Defined as not eating at all.
Grade 3 drowsiness: Defined as prevented normal activity.
Grade 3 fever: Defined as >102.2°F (39.0°C).

f Fever: Defined as ≥100.4°F (38.0°C).

Post-marketing data

Post-marketing experience with FLUARIX and FLUARIX TETRA, which are both manufactured according to the same antigen production and formulation process and are

essentially similar other than FLUARIX lacking a second B-strain, identified the following adverse reactions.[1]

Table 4: FLUARIX TETRA: Adverse reactions observed during post-marketing surveillance

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*, febrile convulsions
Skin and subcutaneous tissue disorders	Rare	Urticaria, pruritus, erythema, angioedema
General disorders and administration site conditions	Rare	Influenza-like illness, malaise, injection-site cellulitis-like reaction

[1]Three of the influenza strains contained in FLUARIX are included in FLUARIX TETRA

*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.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Insufficient data are available.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Pharmacotherapeutic group: Influenza vaccines, ATC Code J07BB02.

FLUARIX TETRA provides active immunisation against the 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 titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HI antibody titers 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 individuals.

Annual revaccination with the current vaccine is recommended because immunity declines during the year after vaccination, and because circulating strains of influenza virus might change from year to year. Protection afforded as a result of vaccination with FLUARIX TETRA is specific to the influenza strains contained in FLUARIX TETRA or to closely related strains.

Clinical trials

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 randomised (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 5.

Table 5: 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	5707	344	6.03	5697	662	11.62	49.8	41.8; 56.8[4]
Culture confirmed	5707	303	5.31	5697	602	10.57	51.2	44.1; 57.6[5]
Culture confirmed vaccine matching strains	5707	88	1.54	5697	216	3.79	60.1	49.1; 69.0[5]
Moderate to Severe Influenza[7]								
RT-PCR confirmed	5707	90	1.58	5697	242	4.25	63.2	51.8; 72.3[4]
Culture confirmed	5707	79	1.38	5697	216	3.79	63.8	53.4; 72.2[5]
Culture confirmed vaccine matching strains	5707	20	0.35	5697	88	1.54	77.6	64.3; 86.6[5]
Lower respiratory Illness RT-PCR Confirmed	5707	28	0.49	5697	61	1.07	54.0	28.9; 71.0[5]
Acute Otitis media RT PCR-confirmed	5707	12	0.21	5697	28	0.49	56.6	16.7; 78.8[5]

[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 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 6), even when there was significant antigenic mismatch with 2 of the vaccine strains (A/H3N2 and B/Victoria).

Table 6: FLUARIX TETRA: Attack rates and vaccine efficacy for RT-PCR confirmed moderate to severe disease by Influenza A subtype and Influenza B lineage 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).

Immunogenicity in children and adults:

Immunogenicity of FLUARIX TETRA was evaluated in terms of HI Geometric mean antibody titer (GMT) at 28 days after the last dose (children) or Day 21 (adults) and HI seroconversion rate (4-fold rise in reciprocal titer or change from undetectable [< 10] to a reciprocal titer 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 7.

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 7.

Table 7: FLUARIX TETRA: Post-vaccination GMT and seroconversion rates 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=1809	N'=1801	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 adjuvanted herpes zoster vaccine (SHINGRIX):

In clinical study Zoster-004, 828 adults without known or suspected immunosuppressive or immunodeficient condition ≥ 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. The antibody responses to each vaccine were similar, whether administered concomitantly or non-concomitantly. Furthermore, 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.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Not applicable.

Distribution

Not applicable.

Metabolism

Not applicable.

Excretion

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

FLUARIX TETRA has not been tested for genotoxic potential.

Carcinogenicity

FLUARIX TETRA has not been tested for carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The vaccine preparation also contains polysorbate 80, octoxinol 10, dl-alpha-tocopheryl acid succinate, sodium chloride, dibasic sodium phosphate dodecahydrate, monobasic potassium phosphate, potassium chloride, magnesium chloride hexahydrate, water for injections.

Residual amounts of ovalbumin ≤0.05 micrograms and formaldehyde ≤5 micrograms, but also traces of gentamicin sulphate, hydrocortisone, and sodium deoxycholate from the manufacturing process may be present.

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 shelf life of FLUARIX TETRA is a maximum of 15 months from the date of manufacture if stored between temperatures of +2^{o}C and +8^{o}C.

The expiry date of the vaccine is indicated on the label and packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

FLUARIX TETRA must be stored between +2°C and +8°C and be protected from light.

DO NOT FREEZE. Discard if vaccine has been frozen.

6.5 NATURE AND CONTENTS OF CONTAINER

FLUARIX TETRA is presented in pre-filled syringes as pack sizes of 1 or 10.

The pre-filled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia requirements.

Not all pack sizes may be distributed in Australia.

FLUARIX TETRA inactivated split influenza vaccine suspension for injection 0.5mL pre-filled PRTC syringe without needle [AUST R 242512]

FLUARIX TETRA inactivated split influenza vaccine suspension for injection 0.5mL pre-filled syringe without needle [AUST R 200674]*

*not currently supplied

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Instructions for use and handling

The vaccine presents as a colourless to slightly opalescent suspension.

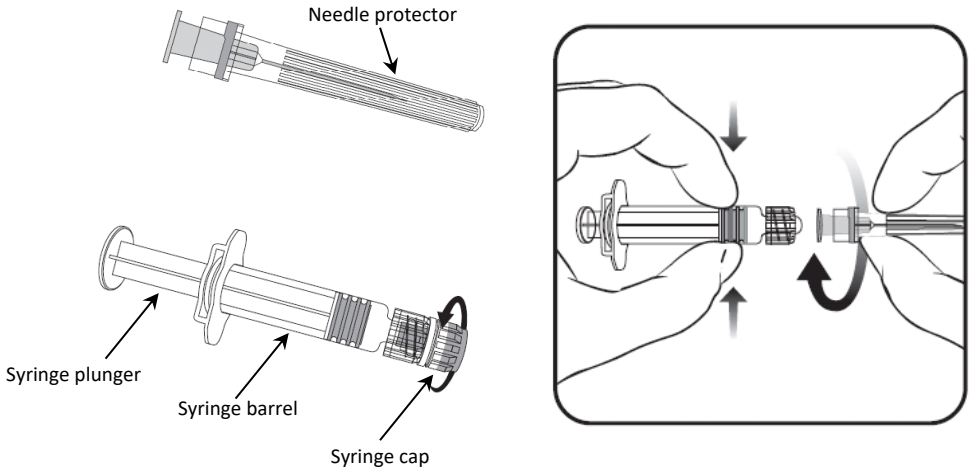
The syringe should be shaken and inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

Instructions for use and handling of the vaccine presented in pre-filled syringe with separate needle:

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

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 product of waste material should be disposed of in accordance with local requirements.

FLUARIX TETRA is for single use in one patient only.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Not applicable.

CAS number

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd
Level 4, 436 Johnston Street,
Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

28 August 2013

10 DATE OF REVISION

6 May 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.5	Addition of information regarding coadministration with adjuvanted herpes zoster vaccine (SHINGRIX)
5.1	Addition of section on concomitant administration with adjuvanted herpes zoster vaccine (Shingrix)

Version 17.0