NEW ZEALAND DATA SHEET

1. PRODUCT NAME

FLUARIX TETRA Quadrivalent influenza vaccine (split virion, inactivated) 0.5 mL suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

FLUARIX TETRA is an inactivated and purified split influenza vaccine. The antigen composition and strains for the 2019 influenza season corresponds to the following types:

A/Michigan/45/2015 (H1N1)pdm09 - like strain (A/Singapore/GP1908/2015, IVR-180)

A/Switzerland/8060/2017 (H3N2) – like strain (A/Brisbane/1/2018, NYMC X-311)
B/Phuket/3073/2013 - like strain (B/Phuket/3073/2013, wild type)

B/Colorado/06/2017 – like strain (B/Maryland/15/2016, NYMC BX-69A)

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 μg haemagglutinin of each of four influenza strains in phosphate buffered saline.

May contain residual amounts of the following process related impurities: hydrocortisone, gentamicin sulphate, ovalbumin, formaldehyde, and sodium deoxycholate.

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 full list of excipients see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

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).

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.

Dose

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.

Children aged <6 months

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

Method of administration

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

For instructions on reconstitution of the medicine before administration, see section 6.6 Special precautions for disposal and other handling.

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.

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.

4.5 Interaction with other medicines and other forms of interaction

FLUARIX TETRA can be concomitantly administered with pneumococcal vaccines (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.

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.

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

Use in older adults

Antibody responses were lower in older adult subjects who received FLUARIX TETRA than in younger subjects. In a randomized, 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.

Effect 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).

4.6 Fertility, pregnancy and lactation

Pregnancy (Category B1)

A reproductive and developmental toxicity study 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, showed no adverse effects on female fertility, pregnancy, parturition, lactation, and embryofoetal and pre-weaning development. Vaccine antigen-specific antibodies were detected in foetuses and pups of treated rats.

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 or maternal outcomes attributable to the vaccine. Therefore, New Zealand's Ministry of Health recommends vaccination for pregnant women at any stage of pregnancy, particularly those who will be in the second or third trimester during the influenza season.

Breastfeeding

FLUARIX TETRA may be used during lactation when the possible advantages outweigh the potential risks.

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.

4.7 Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8 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:

System Organ Class	**Frequency**	**Adverse Reactions**
Nervous System disorder	Common	Headache
	Uncommon	Dizziness[1]
Gastrointestinal disorders	Common	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 sites 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).

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, vomiting, diarrhoea 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 injuration[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	Adverse reaction	Frequency
Blood and lymphatic system disorders	Transient lymphadenopathy	Rare
Immune system disorders	Allergic reactions (including anaphylactic reactions)	Rare
Nervous system disorders	Neuritis, acute disseminated encephalomyelitis, Guillain-Barré syndrome[2]	Rare
Skin and subcutaneous tissue disorders	Urticaria, pruritus, erythema, angioedoema	Rare
General disorders and administration site conditions	Influenza-like illness, malaise	Rare

[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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via: https://nzphvc.otago.ac.nz/reporting.

4.9 Overdose

Insufficient data are available. For advice on the management of overdose, please contact the National Poisons Centre on 0800 POISION (0800 764766).

5. PHARMACOLOGICAL PROPOERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccines, ATC code: J07BB02

Mechanism of action

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

FLUARIX TETRA induces humoral antibodies against the haemagglutinins. These antibodies neutralise influenza viruses.

Specific levels of hemagglutination-inhibition (HI) antibody titre post-vaccination with inactivated influenza virus vaccine 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.

Annual revaccinations with the current vaccine is recommended because immunity declines during the year after vaccination, and because circulating strains of influenza virus might change from years to year

Clinical efficacy and safety

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 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	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 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 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 subcohort of 1,332 children (753 in the FLUARIX TETRA group and 579 in the control group). The results are presented in Table 3.

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 3.

Table 3: 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 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 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.

Immunological non-inferiority has been demonstrated based on published data for all 3 FLUARIX trivalent strains (D-TIV) and all 13-valent pneumococcal conjugate vaccine (PCV13) serotypes in adults 50-59 years of age, as well as for 2 of 3 D-TIV 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 D- TIV as compared to separate administration, however the clinical relevance of this observation is unknown.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

<u>Phosphate buffered saline:</u>

Polysorbate 80
Octoxinol 10
Dl-alpha-tocopheryl hydrogen succinate
Sodium chloride
Dibasic sodium phosphate dodecahydrate
Potassium dihydrogen phosphate
Potassium chloride
Magnesium chloride hexahydrate
Water for Injections

Residues:

Hydrocortisone
Gentamicin sulphate
Ovalbumin
Formaldehyde
Sodium deoxycholate

6.2 Incompatibilities

In the absence of compatibility studies, this medicines must not be mixed with other medicines.

6.3 Shelf life

12 months.

The expiry date of the vaccine is indicated on the label and packaging. The shelf life of FLUARIX TETRA is 12 months from the date of manufacture if stored between temperatures of +2°C and +8°C.

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. Syringes may be supplied with or without a needle. The pre-filled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia requirements.

Latex:

Prefilled syringe with attached needle: the removable rubber needle shield contains natural rubber latex, and therefore this presentation of FLUARIX TETRA Tetra cannot be considered latex-free.

Prefilled syringe with separate needle: the syringe cap, syringe plunger and needle protector of the pre-filled syringes of FLUARIX TETRA with separate needles are not made with natural rubber latex.

6.6 Special precautions for disposal and other handling

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.

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.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

GlaxoSmithKline NZ Limited
Private Bag 106600
Downtown
Auckland
New Zealand

Phone: (09) 367 2900
Facsimile: (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 13 November 2014

10. DATE OF REVISION OF THE TEXT

21 March 2019

Summary table of changes

Section changed	**Summary of new information**
2	Update to 2019 southern hemisphere strain composition
4.6	Addition of information on use in pregnancy, and modification to information on breastfeeding

Version 7.0