

NEW ZEALAND DATA SHEET

Afluria® Quad / Afluria® Quad Junior

For season 2022

1 PRODUCT NAME

Afluria® Quad / Afluria® Quad Junior

Inactivated quadrivalent influenza vaccine (split virion) suspension for injection; containing Influenza virus haemagglutinin as active ingredient.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a purified, inactivated, split virion (split virus) vaccine. Each 0.5 mL dose of Afluria® Quad contains antigens for the 2022 influenza season representative of the following types:

- A/Victoria/2570/2019 (H1N1)pdm09-like virus (A/Victoria/2570/2019 IVR-215):
15 micrograms HA* per dose
 - A/Darwin/9/2021 (H3N2)-like virus (A/Darwin/6/2021 IVR-227):
15 micrograms HA* per dose
 - B/Austria/1359417/2021-like virus (B/Austria/1359417/2021 BVR-26):
15 micrograms HA* per dose
 - B/Phuket/3073/2013-like virus (B/Phuket/3073/2013 BVR-1B):
15 micrograms HA* per dose
- *HA - haemagglutinin

A 0.25 mL dose of Afluria® Quad Junior contains 7.5 micrograms of haemagglutinin of each of the same four influenza strains.

Afluria® Quad / Afluria® Quad Junior is manufactured in eggs and trace amounts of sodium taurodeoxycholate (TDOC) (≤ 5 micrograms per 0.5 mL dose; ≤ 2.5 micrograms per 0.25 mL dose), ovalbumin (< 1 microgram per 0.5 mL dose; < 0.5 microgram per 0.25 mL dose), sucrose, neomycin sulfate, polymyxin B sulfate, propiolactone and hydrocortisone may be present. For the full list of excipients, see **Section 6.1 - LIST OF EXCIPIENTS**.

The type and amount of viral antigens in Afluria® Quad / Afluria® Quad Junior vaccine conform to the requirements of the Australian Influenza Vaccine Committee and the New Zealand Ministry of Health for the winter of 2022. The strains chosen for vaccine

manufacture are endorsed by the Australian Influenza Vaccine Committee as being antigenically equivalent to the reference virus.

The vaccine is prepared from virus grown in the allantoic cavity of embryonated eggs, purified by zonal centrifugation, inactivated by propiolactone and disrupted by sodium taurodeoxycholate.

Afluria® Quad / Afluria® Quad Junior vaccine conforms in safety and sterility to the requirements of the British Pharmacopoeia.

3 PHARMACEUTICAL FORM

Suspension for injection. Afluria® Quad / Afluria® Quad Junior vaccine is a clear to slightly opaque liquid with some sediment that resuspends upon shaking.

See **Section 4.2 - DOSE AND METHOD OF ADMINISTRATION**.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the prevention of influenza caused by Influenza Virus, Types A and B contained in the vaccine. Afluria® Quad vaccine is indicated for use in persons aged 3 years and older.

Afluria® Quad Junior vaccine is indicated for use in children aged 6 months to 35 months inclusive.

See **Section 4.2 - DOSE AND METHOD OF ADMINISTRATION** and **Section 4.4 - SPECIAL WARNINGS AND PRECAUTIONS FOR USE**.

For full details regarding recommendations for influenza vaccination, please refer to the relevant national immunisation guidelines.

4.2 DOSE AND METHOD OF ADMINISTRATION

Immunisation should be undertaken in anticipation of seasonal outbreaks of influenza.

Dose

Table 1: Afluria® Quad / Afluria® Quad Junior Recommended dosage, by age group

Age Group	Presentation	Dose	Number of Doses
Paediatrics			
6 months to 35 months	Afluria® Quad Junior	0.25 mL	1 or 2 ^a

3 years to < 9 years	Afluria® Quad	0.5 mL	1 or 2 ^a
9 to < 18 years	Afluria® Quad	0.5 mL	1
Adults			
≥ 18 years	Afluria® Quad	0.5 mL	1

^a Previously unvaccinated children 6 months to < 9 years of age should be given 2 doses at least 4 weeks apart

To provide continuing protection, annual vaccination with vaccine containing the most recent strains is necessary.

Method of administration

Afluria® Quad / Afluria® Quad Junior vaccine should be administered by a healthcare practitioner in an appropriate setting with an appropriate post-vaccination observation period.

Shake before use. After shaking, the vaccine should appear as a homogenous suspension. The vaccine must be inspected visually prior to administration and should not be used if there is any variation of physical appearance.

See **Section 3 - PHARMACEUTICAL FORM.**

The vaccine should be administered by intramuscular or deep subcutaneous injection.

Afluria® Quad / Afluria® Quad Junior vaccine can be administered concurrently with other vaccines, however separate syringes and a separate arm should be used.

Persons with a history of egg allergy (non-anaphylaxis) can receive an age-appropriate full dose of vaccine in any immunisation setting [See also **Section 4.4 - SPECIAL WARNINGS AND PRECAUTIONS FOR USE**].

Each pre-filled syringe is for use in one patient on one occasion only. Discard any residue.

4.3 CONTRAINDICATIONS

Afluria® Quad and Afluria® Quad Junior vaccine are contraindicated in children less than 6 months of age because the safety and efficacy in this age group has not been established.

Afluria® Quad and Afluria® Quad Junior vaccine are contraindicated in individuals who have previously experienced:

- Anaphylaxis following a dose of any influenza vaccine

- Anaphylaxis following exposure to any component of the vaccine, excluding egg protein [See **Section 2 - QUALITATIVE AND QUANTITATIVE COMPOSITION** and **Section 4.4 - SPECIAL WARNINGS AND PRECAUTIONS FOR USE**]

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The safety and efficacy of Afluria® Quad vaccine in children less than 6 months of age has not been established in clinical trials.

As with other injectable vaccines, appropriate medical treatment and supervision should always be available to manage the rare event of an anaphylactic reaction following administration of the vaccine. Persons with a history of anaphylaxis to egg should be vaccinated only in medical facilities with staff experienced in recognising and treating anaphylaxis. For full details regarding recommendations for influenza vaccination in individuals with egg allergy, please refer to the relevant national immunisation guidelines.

Adrenaline should always be ready for immediate use whenever any injection is given. Immunisation should be postponed in patients with acute febrile illness until the fever is resolved. In immunocompromised patients the antibody response may be lower.

If Guillain-Barré syndrome has occurred within 6 weeks of previous influenza vaccination, the decision to give Afluria® Quad / Afluria® Quad Junior vaccine should be based on careful consideration of the potential benefits and risks.

Paediatric Use

The safety and efficacy of Afluria® Quad / Afluria® Quad Junior vaccine in persons less than 6 months of age has not been established in clinical trials.

Afluria® Quad /Afluria® Quad Junior vaccine was administered in children 6 months to < 5 years of age in clinical study QIV-03 (N = 1673) (See **Section 4.8 - UNDESIRABLE EFFECTS** and **Section 5.1 - PHARMACODYNAMIC PROPERTIES – Clinical trial data**).

In subjects 6 months to < 3 years of age administered Afluria® Quad Junior vaccine, the most common local adverse reactions experienced by $\geq 10\%$ subjects were injection site pain (20.8%) and injection site redness (20.8%). The most common systemic adverse event experienced by $\geq 10\%$ subjects were irritability (32.9%), diarrhoea (24.2%) and loss of appetite (20.0%).

In subjects 3 to < 5 years of age administered Afluria® Quad vaccine, the most common

local adverse reactions experienced by $\geq 10\%$ subjects were injection site pain (35.5%), injection site redness (22.4%) and injection site swelling/ induration (10.1%). The most common systemic adverse events experienced by $\geq 10\%$ subjects were malaise and fatigue (14.3%), and diarrhoea (12.1%).

Afluria® Quad was administered to children 5 to < 18 years of age in clinical study QIV-02 (N = 1692) (See **Section 4.8 - UNDESIRABLE EFFECTS** and **Section 5.1 - PHARMACODYNAMIC PROPERTIES – Clinical trial data**).

In subjects 5 to < 9 years of age administered Afluria® Quad vaccine, the most common local adverse reactions experienced by $\geq 10\%$ subjects were injection site pain (51.3%), injection site erythema (19.4%), and injection site swelling/induration (15.3%). The most common systemic adverse event experienced by $\geq 10\%$ subjects was headache (12.3%).

In subjects 9 to < 18 years of age administered Afluria® Quad vaccine, the most common local adverse reactions experienced by $\geq 10\%$ subjects were injection site pain (51.5%), injection site erythema (14.8%), and injection site swelling/induration (12.2%). The most common systemic adverse events experienced by $\geq 10\%$ subjects were headache (18.8%), myalgia (16.7%) and malaise and fatigue (10.0%).

Use in the Elderly

The safety and immunogenicity of Afluria® Quad vaccine was evaluated in adults ≥ 65 years in QIV-01 (See **Section 4.8 - UNDESIRABLE EFFECTS** and **Section 5.1 - PHARMACODYNAMIC PROPERTIES – Clinical trial data**). There were 541 enrolled subjects aged 65 to < 75 years and 329 enrolled subjects ≥ 75 years. Antibody responses to Afluria® Quad vaccine were non-inferior to comparator trivalent influenza (TIV-1 and TIV-2) responses in adults ≥ 65 years of age, and lower than in younger adults.

Effect on Laboratory Tests

Interference of Afluria® Quad / Afluria® Quad Junior vaccine with laboratory and/or diagnostic tests has not been studied.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

No interaction studies have been performed on interaction between influenza vaccines in general and other vaccines or medications.

4.6 FERTILITY, PREGNANCY AND LACTATION EFFECTS ON FERTILITY

Afluria® Quad / Afluria® Quad Junior vaccine has not been evaluated for possible effect on fertility.

A reproductive study of female rats vaccinated with Seqirus' trivalent influenza vaccine (Fluvax®) revealed no impairment of fertility.

Use in Pregnancy: Category A

No embryofetal development study has been conducted with Afluria® Quad vaccine. A rat reproduction study has been conducted with Seqirus' trivalent influenza vaccine (Fluvax®). This study did not demonstrate any maternal or developmental toxicity.

Influenza vaccination is recommended for pregnant women during any stage of pregnancy. This recommendation is based on the known adverse consequences of influenza infection during pregnancy and the large body of data showing that large numbers of women have been vaccinated during pregnancy with inactivated influenza vaccines with no increased risk of adverse fetal or maternal outcomes attributable to the vaccine. Afluria® Quad vaccine should be given to pregnant women following an assessment of the risks and benefits.

Use in Lactation

The safety and effectiveness of Afluria® Quad vaccine has not been established in nursing mothers.

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 machinery.

4.8 UNDESIRABLE EFFECTS

Clinical trials:

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to rates in the clinical studies of another vaccine and may not reflect the rates of events observed in clinical practice.

Three clinical studies with Afluria® Quad / Afluria® Quad Junior vaccine have been completed.

QIV-01 (NCT02214225, see <http://clinicaltrials.gov>) was a randomised, double-blind, active- controlled trial conducted in the US in 3449 subjects aged ≥ 18 years. Subjects in the safety population received one dose of either Afluria® Quad vaccine (N = 1721) or one of two formulations of comparator trivalent influenza vaccine (TIV-1 N = 864 or TIV-2 N = 864) each containing an influenza type B virus that corresponded to one of the two B viruses in Afluria® Quad vaccine (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage).

Local (injection-site) adverse reactions and systemic adverse events were solicited for 7 days post- vaccination (Table 2). Unsolicited adverse events were collected for 28 days post-vaccination. Serious adverse events were collected for 180 days post-vaccination. All adverse events are presented regardless of any treatment causality assigned by study investigators.

QIV-02 (NCT02545543, see <http://clinicaltrials.gov>) was a randomised, observer-blind, comparator-controlled trial that evaluated the immunogenicity and safety of Afluria® Quad vaccine in subjects aged 5 to < 18 years with a 2015-2016 comparator quadrivalent influenza vaccine. Study subjects were scheduled to receive either a single vaccination or two-vaccination regime as clinically indicated. Local (injection site) adverse reactions and systemic adverse events were solicited for 7 days post vaccination (Table 3). Unsolicited adverse events and cellulitis-like reactions at the injection site were collected for 28 days after the last vaccination; and serious adverse events for six months following last vaccination.

QIV-03 (NCT02914275, see <http://clinicaltrials.gov>) was a randomised, observer-blind, comparator controlled trial that evaluated the immunogenicity and safety of Afluria® Quad / Afluria® Quad Junior vaccine in subjects ages 6 months to < 5 years with a 2016-2017 comparator quadrivalent influenza vaccine. Study subjects were scheduled to receive either a single vaccination or two-vaccination regimen as clinically indicated. Local (injection site) adverse reactions and systemic adverse events were solicited for 7 days post-vaccination (Table4).

Unsolicited adverse events and cellulitis-like reactions at the injection site were collected for 28 days after the last vaccination; and serious adverse events for six months following last vaccination.

Adult data

In adults 18 to < 65 years, the most commonly reported injection-site adverse reaction observed in clinical studies with Afluria® Quad vaccine was pain ($\geq 40\%$). The most common systemic adverse events observed were myalgia and headache ($\geq 20\%$). In adults

≥ 65 years of age, the most commonly reported injection-site adverse reaction observed in clinical studies with Afluria® Quad vaccine was pain (≥ 20%). The most common systemic adverse event observed was myalgia (≥ 10%). A small number of adults ≥ 65 years of age (N = 4) experienced severe injection site swelling.

Table 2: QIV-01: Proportion of Subjects per Age Cohort with Any Solicited Local Adverse Reactions or Systemic Adverse Events within 7 Days after Administration of Afluria® Quad vaccine or Trivalent Influenza vaccine (TIV-1 or TIV-2), Irrespective of Causality (Safety population)

	Percentage (%) ^a of Subjects in each Age Cohort Reporting an Event											
	Subjects 18 to < 65 years						Subjects ≥ 65 years					
	Afluria® Quad vaccine N=854 ^b		TIV-1 N=428 ^b		TIV-2 N=430 ^b		Afluria® Quad vaccine N=867 ^b		TIV-1 N=436 ^b		TIV-2 N=434 ^b	
	Any	Gr 3	Any	Gr 3	Any	Gr 3	Any	Gr 3	Any	Gr 3	Any	Gr 3
Local Adverse Reactions^c												
Pain	47.9	0.7	43.7	1.4	50.7	1.2	24.6	0.1	22.7	0	21.0	0.2
Swelling/Lump	3.7	0.1	2.3	0	3.5	0.2	3.2	0.5	1.8	0	1.6	0
Redness	2.9	0	2.8	0	2.8	0	4.2	0.3	2.1	0	2.5	0.2
Systemic Adverse Events^d												
Myalgia (muscle ache)	25.5	1.9	23.4	1.4	24.2	1.2	12.7	0.3	14.0	0.7	12.2	0.5
Headache	21.7	1.7	15.2	0.9	19.1	1.2	8.4	0	7.1	0.2	7.8	0.7
Malaise	8.9	0.7	9.1	0	9.3	0.7	4.4	0.5	5.0	0.2	5.1	0.2
Nausea	6.9	0.6	7.7	0.5	6.3	1.2	1.6	0	1.8	0	2.1	0.2
Chills	4.8	0.6	4.4	0.2	4.7	0.5	2.0	0	2.1	0.5	1.4	0.2
Vomiting	1.5	0.4	0.9	0	2.3	0.7	0.5	0.1	0	0	0.7	0.2
Fever	1.1	0.4	0.9	0	0.5	0	0.2	0	0.9	0	0.5	0.2

Abbreviations: Gr3, Grade 3

^a Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by study vaccine group, based on the number of subjects contributing any follow up safety information for at least one data value of an individual sign/symptom.

^b N = number of subjects in the Safety Population Subgroup for each study vaccine group.

^c Local adverse reactions: Grade 3 pain is that which prevents daily activity; Swelling/Lump and redness: any = ≥ 20 mm diameter, Grade 3 = ≥ 100 mm diameter

^d Systemic adverse events: Fever: any = ≥ 38.0°C (Oral), Grade 3 = ≥ 39.0°C (Oral); Grade 3 for all other adverse events is that which prevents daily activity.

In adults 18 to < 65 years who received Afluria® Quad vaccine, commonly reported unsolicited adverse events were headache (5.3%), oropharyngeal pain (2.5%), back pain (1.9%), diarrhoea (1.6%), cough (1.3%) and nausea (1.1%). In adults ≥ 65 years who received Afluria® Quad vaccine, commonly reported unsolicited adverse events were headache (2.3%), rhinorrhoea (1.3%), oropharyngeal pain (1.2%) and back pain (1.2%).

Paediatric data: 5 years to < 18 years of age

Afluria® Quad vaccine was administered to children 5 to < 18 years of age in Study QIV-02.

In children 5 to < 18 years, the most common ($\geq 10\%$) injection site reactions were pain (51.4%), redness (17.1%), and induration/swelling (13.8%); the most common solicited systemic adverse events were headache (15.5%) and myalgia (13.1%).

Table 3: QIV-02: Proportion of Subjects Per Age Cohort with Any Solicited Local Adverse Reactions or Systemic Adverse Events within 7 Days after Administration of Afluria® Quad Vaccine or Comparator QIV

	Percentage (%) ^a of Subjects in each Age Cohort Reporting an Event							
	Subjects 5 to < 9 years				Subjects 9 to < 18 years			
	Afluria® Quad vaccine N=829 ^b		Comparator QIV N=274 ^b		Afluria® Quad vaccine N=792 ^b		Comparator QIV N=261 ^b	
	Any	Gr 3	Any	Gr 3	Any	Gr 3	Any	Gr 3
Local Adverse Reactions^c								
Pain	51.3	0.8	49.6	0.7	51.5	0.3	45.2	0.4
Redness	19.4	3.5	18.6	1.8	14.8	1.9	16.1	1.9
Swelling/Lump	15.3	3.4	12.4	2.2	12.2	2.0	10.7	1.9
Systemic Adverse Events^d								
Headache	12.3	0.1	10.6	0.4	18.8	0.4	14.6	0.4
Myalgia	9.8	0.1	11.3	0.4	16.7	0.3	11.1	0.4
Malaise and	8.8	0.4	5.8	0	10.0	0.4	7.7	0
Nausea	7.1	0.1	8.4	0	7.7	0	8.0	0
Diarrhoea	5.2	0	3.6	0	5.4	0	4.2	0
Fever	4.5	1.2	3.6	0.7	2.1	0.5	0.8	0
Vomiting	2.4	0.2	4.4	0	1.8	0	2.3	0

Abbreviations: Gr 3, Grade 3; Comparator QIV, Fluarix® Quadrivalent [GlaxoSmithKline Biologicals]

^a Percent (%) is derived from the number of subjects that reported the event divided by the Solicited Safety Population in each vaccine group and age cohort.

^b N = number of subjects in the Solicited Safety Population (subjects who were vaccinated and provided any solicited safety data) for each study vaccine group. Solicited Safety Population was the same for each event.

^c Local adverse reactions: Grade 3 pain is that which prevents daily activity; Swelling/Lump and redness: any = > 0 mm diameter, Grade 3 = > 30 mm diameter.

^d Systemic adverse events: Fever: any = $\geq 38.0^\circ\text{C}$ (Oral), Grade 3 = $\geq 39.0^\circ\text{C}$ (Oral); Grade 3 for all other adverse events is that which prevents daily activity.

There were no vaccine-related deaths reported in this paediatric study QIV-02. There was one vaccine-related serious adverse event (influenza) reported in this study.

One subject experienced a cellulitis-like reaction (defined as concurrent severe pain, redness and swelling) at the injection site after vaccination with Afluria® Quad vaccine.

In children 5 to < 18 years administered Afluria® Quad vaccine, cough (2.1%) was the most commonly reported unsolicited adverse event. Other commonly reported unsolicited adverse events (reported by $\geq 1\%$ of subjects) were oropharyngeal pain (1.3%), pyrexia (1.3%) and upper respiratory tract infection (1.1%).

The most commonly reported unsolicited adverse events among subjects who received Afluria® Quad vaccine in ages 5 to < 9 years following the first or second dose included cough (2.8%), pyrexia (2.1%), headache (1.2%), rhinorrhoea (1.2%), upper respiratory tract infection (1.2%), influenza-like illness (1.0%), and oropharyngeal pain (1.0%).

For subjects aged 9 to < 18 years who received Afluria® Quad vaccine, the most common unsolicited adverse events included oropharyngeal pain (1.6%), cough (1.3%), and upper respiratory tract infection (1.0%).

Paediatric data: 6 months to < 5 years of age

Afluria® Quad / Afluria® Quad Junior vaccine was administered to children 6 months to < 5 years of age in Study QIV-03.

In children 6 months to < 3 years of age, the most common ($\geq 10\%$) injection site reactions were pain (20.8%) and redness (20.8%); the most common solicited systemic adverse events were irritability (32.9%), diarrhoea (24.2%) and loss of appetite (20.0%).

In children 3 to < 5 years of age, the most common ($\geq 10\%$) injection site reactions were pain (35.5%), redness (22.4%) and swelling (10.1%); the most common solicited systemic adverse events were malaise and fatigue (14.3%) and diarrhoea (12.1%).

Table 4: QIV-03: Proportion of Subjects Per Age Cohort with Any Solicited Local Adverse Reactions or Systemic Adverse Events within 7 Days after Administration of Afluria® Quad/ Afluria® Quad Junior vaccine or Comparator QIV

	Percentage (%) ^a of Subjects in each Age Cohort Reporting an Event							
	6 months to < 3 years				3 to <5 years			
	Afluria® Quad Junior vaccine N= 669 ^b		Comparator QIV N= 227 ^b		Afluria® Quad vaccine N= 949 ^b		Comparator QIV N= 318 ^b	
	Any	Gr 3	Any	Gr 3	Any	Gr 3	Any	Gr 3
Local Adverse Reactions^c								
Pain	20.8	0.1	25.6	0.4	35.5	0	31.4	0.6
Redness	20.8	0.6	17.6	1.8	22.4	2.3	20.8	5.3
Swelling/Lump	6.1	0.4	6.2	0.9	10.1	1.7	12.9	2.5
Systemic Adverse Events^d								
Irritability	32.9	0.7	28.2	0.4	-	-	-	-
Diarrhoea	24.2	0.1	25.6	0.4	12.1	0.1	8.8	0.6
Loss of Appetite	20.0	0.3	19.4	0.4	-	-	-	-
Malaise and Fatigue	-	-	-	-	14.3	0.5	13.2	0.3
Myalgia	-	-	-	-	9.9	0.1	9.4	0
Nausea and/or vomiting	9.4	0.7	11.0	0	9.2	0.4	6.6	0.3
Headache	-	-	-	-	6.2	0.4	5.0	0
Fever	7.2	2.5	11.9	2.6	4.8	1.2	6.0	0.9

Abbreviations: Gr 3, Grade 3; Comparator QIV, Fluzone® Quadrivalent QIV [Sanofi Aventis]

^a Percent (%) is derived from the number of subjects that reported the event divided by the Solicited Safety Population in each vaccine group and age cohort.

^b N = number of subjects in the Solicited Safety Population (subjects who were vaccinated and provided any solicited safety data) for each study vaccine group. Solicited Safety Population was the same for each event.

^c Local adverse reactions: Grade 3 pain is that which prevents daily activity (3 to < 5 years subjects); or cried when limb was moved or spontaneously painful (6 months to < 3 years subjects); Swelling/Lump and redness: any = ≥ 0mm diameter, Grade 3 = ≥ 30mm diameter.

^d Systemic adverse events: Fever: any = ≥ 37.5°C (Axillary), Grade 3 = ≥ 38.5°C (Axillary); Grade 3 for all other adverse events is that which prevents daily activity; Irritability, Loss of Appetite, Malaise and Fatigue, Myalgia and Headache are age specific systemic adverse events, where “-” denotes event was not applicable to that age cohort.

There were no vaccine-related deaths or vaccine-related serious adverse events reported in this paediatric study QIV-03.

In children 6 months to < 5 years administered Afluria® Quad/ Afluria® Quad Junior vaccine, cough (9.1%) was the most commonly reported unsolicited adverse event. Other commonly reported unsolicited adverse events (reported by ≥ 1% of subjects) were rhinorrhoea (8.0%), pyrexia (5.4%), upper respiratory tract infection (4.0%), vomiting

(2.5%), diarrhoea (2.3%), otitis media (2.2%), nasal congestion (2.1%), nasopharyngitis (1.8%), irritability (1.2%), fatigue (1.1%) and rash (1.0%).

The most commonly reported unsolicited adverse events among subjects who received Afluria® Quad Junior vaccine in ages 6 months to < 3 years following the first or second dose included rhinorrhoea (12.1%), cough (11.0%), pyrexia (6.6%), upper respiratory tract infection (5.9%), diarrhoea (4.0%), otitis media (3.6%), vomiting (2.7%), nasal congestion (2.4%), nasopharyngitis (1.9%), irritability (1.7%), ear infection (1.6%), croup infections (1.4%), teething (1.3%), rash (1.3%), dermatitis diaper (1.3%), influenza like illness (1.2%) and fatigue (1.0%).

For subjects ages 3 to < 5 years who received Afluria® Quad vaccine, the most common unsolicited adverse events included cough (7.9%), rhinorrhoea (5.1%), pyrexia (4.6%), upper respiratory tract infection (2.7%), vomiting (2.3%), nasal congestion (1.8%), nasopharyngitis (1.7%), oropharyngeal pain (1.2%) diarrhoea (1.1%), otitis media (1.1%), headache (1.1%), and fatigue (1.1%).

Post-marketing surveillance:

There are limited post-marketing data available for Afluria® Quad Junior vaccine.

The Afluria® Quad / Afluria® Quad Junior vaccine formulation is based on Seqirus' trivalent influenza (Fluvax®), with the exception of an additional B influenza strain.

The adverse events spontaneously reported during post-approval use of Fluvax® and/or Afluria® Quad are presented below.

Blood and Lymphatic System Disorders

Thrombocytopenia.

Immune System Disorders

Allergic or immediate hypersensitivity reactions including anaphylactic shock.

Nervous System Disorders

Neuralgia, paraesthesia and convulsions (including febrile convulsions), dizziness, encephalomyelitis, neuritis or neuropathy, and Guillain-Barré syndrome.

Vascular Disorders

Vasculitis which may be associated with renal involvement.

Musculoskeletal and Connective Tissue Disorders

Musculoskeletal pain and pain in extremity.

Skin and Subcutaneous Tissue Disorders

Pruritus, urticaria and rash.

General Disorders and Administration Site Conditions

Cellulitis and large injection site swelling, Influenza-like illness, injected limb mobility decreased, pyrexia, injection site erythema and injection site reaction.

Reporting 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 using the following website <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

There is no specific information on overdose of influenza vaccines.

For general advice on overdose management:

In Australia, contact the Poisons Information Centre on 131 126.

In New Zealand, call the New Zealand Poisons Centre on 0800 POISON or 0800 764 766.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Influenza Vaccines ATC Code: J07B B02

Pharmacodynamic effects

Afluria® Quad / Afluria® Quad Junior vaccine has been shown to induce antibodies to the viral surface glycoprotein, haemagglutinin. These antibodies are important in the prevention of natural infection.

Specific levels of haemagglutination inhibition (HI) antibody titres post-vaccination with inactivated influenza vaccine have not been correlated with protection from influenza virus. In some human studies, antibody titres of 1:40 or greater have been associated with

protection from influenza illness in up to 50% of subjects. Antibodies against one influenza virus type or subtype confers limited or no protection against another. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype.

Annual revaccination with the current vaccine is recommended because immunity declines during the year after vaccination and circulating strains of influenza virus change from year to year.

Clinical trial data

Adult Studies

One clinical study has been completed with Afluria® Quad vaccine on adults 18 years and older.

QIV-01 (NCT02214225, see <http://clinicaltrials.gov>) was a randomised, double-blind, active comparator-controlled trial conducted in the US in adults aged 18 years and older. Subjects in the per protocol population that was used for the primary immunogenicity analysis received one dose of either Afluria® Quad vaccine (N = 1691) or one of two formulations of comparator trivalent influenza vaccine (TIV-1 N = 854 or TIV-2 N = 850), each containing an influenza type B virus that corresponded to one of the two B viruses in Afluria® Quad vaccine (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). The mean age of the enrolled population was 58 years. 57% were female, 82% were White and 16% Black/African American. The age sub- groups were 18 to < 65 years and ≥ 65 years with a mean age of 43 years and 73 years, respectively. Post-vaccination immunogenicity was evaluated on sera obtained 21 days after administration of a single dose of Afluria® Quad vaccine or TIV.

The co-primary endpoints were HI Geometric Mean Titre (GMT) ratios (adjusted for baseline HI titres) and the difference in seroconversion rates for each vaccine strain, 21 days after the vaccination. Pre-specified non-inferiority criteria required that the upper bound of the 2-sided 95% CI of the GMT ratio (TIV/Afluria® Quad vaccine) did not exceed 1.5 and the upper bound of the 2- sided 95% CI of the seroconversion rate difference (TIV minus Afluria® Quad vaccine) did not exceed 10% for each strain.

Serum HI antibody responses to Afluria® Quad vaccine were non-inferior to both TIVs for all influenza strains. Additionally, non-inferiority was demonstrated for both endpoints in both age sub- groups, adults aged 18 to < 65 years and ≥ 65 years (Table 5), for all strains. Antibody responses were lower in adults aged ≥ 65 years.

Superiority of the immune response to each of the influenza B strains contained in

Afluria® Quad vaccine was shown relative to the antibody response after vaccination with TIV formulations not containing that B lineage strain. Superiority against the alternate B strain was also demonstrated for each of the influenza B strains in both age sub-groups; 18 to < 65 years and ≥ 65 years.

Post-hoc analyses of immunogenicity by gender did not demonstrate significant differences between males and females. The study population was not sufficiently diverse to assess differences between races or ethnicities.

Table 5: QIV-01: Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and Analyses of Non-Inferiority of Afluria® Quad vaccine Relative to Trivalent Influenza Vaccine (TIV) for each Strain, at 21 Days Post-Vaccination by Age Cohort (Per Protocol Population)

Strain	Post-vaccination GMT ^a		GMT Ratio	Seroconversion % ^b		Difference	Met both pre-defined non-inferiority criteria? ^c
	Afluria® Quad vaccine	Pooled TIV or TIV-1 (B Yam) or TIV-2 (B Vic)	Pooled TIV or TIV-1 or TIV-2 over Afluria® Quad vaccine (95% CI)	Afluria® Quad vaccine	Pooled TIV or TIV-1 (B Yam) or TIV-2 (B Vic)	Pooled TIV or TIV-1 or TIV-2 minus Afluria® Quad vaccine (95% CI)	
18 to < 65 years	Afluria® Quad vaccine N=835, Pooled TIV N=845, TIV-1 N=424, TIV-2 N=421						
A/H1N1	432.7	402.8	0.93 ^d (0.85, 1.02)	51.3	49.1	-2.1 ^g (-6.9, 2.7)	Yes
A/H3N2	569.1	515.1	0.91 ^d (0.83, 0.99)	56.3	51.7	-4.6 ^g (-9.4, 0.2)	Yes
B/YAM	92.3	79.3	0.86 ^e (0.76, 0.97)	45.7	41.3	-4.5 ^h (-10.3, 1.4)	Yes
B/VIC	110.7	95.2	0.86 ^f (0.76, 0.98)	57.6	53.0	-4.6 ⁱ (-10.5, 1.2)	Yes
≥ 65 years	Afluria® Quad vaccine N=856, Pooled TIV N=859, TIV-1 N=430, TIV-2 N=429						
A/H1N1	211.4	199.8	0.95 ^d (0.88, 1.02)	26.6	26.4	-0.2 ^g (-5.0, 4.5)	Yes
A/H3N2	419.5	400.0	0.95 ^d (0.89, 1.02)	25.9	27.0	1.1 ^g (-3.7, 5.8)	Yes
B/YAM	43.3	39.1	0.90 ^e (0.84, 0.97)	16.6	14.4	-2.2 ^h (-8.0, 3.6)	Yes
B/VIC	66.1	68.4	1.03 ^f (0.94, 1.14)	23.5	24.7	1.2 ⁱ (-4.6, 7.0)	Yes

Abbreviations: CI, confidence interval; GMT, geometric mean titre.

^a GMT results were modelled on a multi-variable adjusted analysis including gender, vaccination history, pre-vaccination HI modelled and other factors.

^b Seroconversion rate is defined as a 4-fold increase in post-vaccination HI antibody titre from pre-vaccination titre $\geq 1:10$ or an increase in titre from $< 1:10$ to $\geq 1:40$.

^c Non-inferiority (NI) criteria for the GMT ratio: upper bound of 2-sided 95% CI on the ratio of Pooled TIV or TIV-1 (B Yamagata) or TIV-2 (B Victoria)/ Afluria® Quad vaccine. GMT should not exceed 1.5. NI criteria for the seroconversion rate (SCR) difference: upper bound of 2-sided 95% CI on the difference between SCR Pooled TIV or TIV-1 (B Yamagata) or TIV-2 (B Victoria) minus Afluria® Quad vaccine should not exceed 10%.

^d Pooled TIV/Afluria® Quad vaccine

^e TIV-1 (B Yamagata)/Afluria® Quad vaccine

^f TIV-2 (B Victoria)/Afluria® Quad vaccine

^g Pooled TIV - Afluria® Quad vaccine

^h TIV-1 (B Yamagata) - Afluria® Quad vaccine

ⁱ TIV-2 (B Victoria) - Afluria® Quad vaccine

Paediatric studies

5 to < 18 years of age

One clinical study has been completed with Afluria® Quad vaccine in children aged 5 to < 18 years of age.

QIV-02 (NCT02545543, see <http://clinicaltrials.gov>) was a randomised, observer-blinded, comparator-controlled trial conducted in the US in children 5 to < 18 years of age.

Subjects received either one or two doses of either Afluria® Quad vaccine (N = 1 605) or a comparator quadrivalent influenza vaccine (N = 528) in a 3:1 randomisation treatment schedule. Subjects 5 to < 9 years of age were eligible to receive a second dose at least 28 days after the first dose depending on their influenza vaccination history. Approximately 25% of subjects in each treatment group in the 5 to < 9 years of age sub-group received two vaccine doses. Baseline serology prior to vaccination and sera obtained 28 days after the last vaccination dose was collected and immunogenicity was evaluated by HI assay.

The co-primary endpoints were HI Geometric Mean Titres (GMT) (adjusted for baseline HI titres and other covariates) and seroconversion rates for each vaccine strain, 28 days after the last vaccination. Pre-specified non-inferiority criteria required that the upper bound of the 2-sided 95% CI of the GMT ratio (Comparator QIV/Afluria® Quad vaccine) did not exceed 1.5 and the upper bound of the 2-sided 95% CI of the seroconversion rate difference (Comparator QIV minus Afluria® Quad vaccine) did not exceed 10% for each strain.

Serum HI antibody responses to Afluria® Quad vaccine were non-inferior for both GMT and seroconversion rates relative to the Comparator QIV for all influenza strains (Table 6). Analyses of immunogenicity endpoints by gender did not demonstrate meaningful

differences between males and females. The study population was not sufficiently diverse to assess differences between races or ethnicities.

Table 6: QIV-02: Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and Analyses of Non-Inferiority of Afluria® Quad Vaccine Relative to Comparator QIV for each Strain 28 Days after Last Vaccination Among a Paediatric Population 5 to < 18 Years of Age (Per Protocol Population)^f

Strain	Post-vaccination GMT		GMT Ratio ^a	Seroconversion % ^b		Difference ^c	Met both pre-defined non-inferiority criteria? ^d
	Afluria® Quad vaccine N=1605	Comparator QIV N=528	Comparator QIV over Afluria® Quad vaccine (95% CI)	Afluria® Quad vaccine N=1605 (95% CI)	Comparator QIV N=528 (95% CI)	Comparator QIV minus Afluria® Quad vaccine (95% CI)	
A/H1N1	952.6 (n=1604 ^e)	958.8	1.01 (0.93, 1.09)	66.4 (64.0, 68.7)	63.3 (59.0, 67.4)	-3.1 (-8.0, 1.8)	Yes
A/H3N2	886.4 (n=1604 ^e)	930.6	1.05 (0.96, 1.15)	82.9 (81.0, 84.7)	83.3 (79.9, 86.4)	0.4 (-4.5, 5.3)	Yes
B/YAM	60.9 (n=1604 ^e)	54.3	0.89 (0.81, 0.98)	58.5 (56.0, 60.9)	55.1 (50.8, 59.4)	-3.4 (-8.3, 1.5)	Yes
B/VIC	145.0 (n=1604 ^e)	133.4	0.92 (0.83, 1.02)	72.1 (69.8, 74.3)	70.1 (66.0, 74.0)	-2.0 (-6.9, 2.9)	Yes

Abbreviations: B/VIC, B Victoria lineage; B/YAM, B Yamagata lineage; CI, confidence interval; Comparator QIV, Fluarix® Quadrivalent [GlaxoSmithKline Biologicals]; GMT (adjusted), geometric mean titre.

^a GMT Ratio = Comparator QIV / Afluria® Quad vaccine. Adjusted analysis model: Log-transformed Post-Vaccination HI Titre = Vaccine

+ Age Strata [5-8, 9-17] + Gender + Vaccination History [y/n] + Log-transformed Pre-Vaccination HI Titre + Site + Number of Doses (1 vs 2) + Age Strata*Vaccine. The Age Strata*Vaccine interaction term was excluded from the model fit for the strains B/Yamagata and B/Victoria as the interaction result was non-significant (p > 0.05). Least square means were back transformed.

^b Seroconversion rate (SCR) was defined as the percentage of subjects with either a pre-vaccination HI titre < 1:10 and a post-vaccination

HI titre ≥ 1:40 or a pre-vaccination HI titre ≥ 1:10 and a 4-fold increase in post-vaccination HI titre.

^c Seroconversion rate difference = Comparator QIV SCR percentage minus Afluria® Quad vaccine SCR percentage.

^d Non-inferiority (NI) criterion for the GMT ratio: upper bound of two-sided 95% CI on the GMT ratio of Comparator QIV/QIV should not exceed 1.5. NI criterion for the SCR difference: upper bound of two-sided 95% CI on the difference between SCR Comparator QIV – Afluria® Quad vaccine should not exceed 10%.

^e Subject 8400394-0046 was excluded from the Per-Protocol Population for the adjusted GMT analysis for the GMT ratio since the subject did not have information on all covariates (unknown pre-vaccination history).

^f The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results.

6 months to < 5 years of age

One clinical study has been completed with Afluria® Quad / Afluria® Quad Junior vaccine in children aged 6 months to < 5 years of age.

QIV-03 (NCT02914275, see <http://clinicaltrials.gov>) was a randomised, observer blinded, comparator-controlled trial conducted in the US in children 6 months to < 5 years of age. A total of 2247 subjects were randomised 3:1 to receive one or two doses of Afluria® Quad / Afluria® Quad Junior (N = 1684) or a comparator quadrivalent influenza vaccine (N = 563). Subjects were eligible to receive a second dose at least 28 days after the first dose depending on their influenza vaccination history. Approximately 40% of subjects in each treatment group received two vaccine doses. Baseline serology prior to vaccination and sera obtained 28 days after the last vaccination dose was collected and immunogenicity was evaluated by HI assay.

The co-primary endpoints were HI Geometric Mean Titres (GMT) (adjusted for baseline HI titres and other covariates) and seroconversion rates for each vaccine strain, 28 days after the last vaccination. Pre-specified non-inferiority criteria required that the upper bound of the 2-sided 95% CI of the GMT ratio (Comparator QIV/Afluria® Quad vaccine) did not exceed 1.5 and the upper bound of the 2-sided 95% CI of the seroconversion rate difference (Comparator QIV minus Afluria® Quad vaccine) did not exceed 10% for each strain.

Serum HI antibody responses to Afluria® Quad vaccine were non-inferior for both GMT and seroconversion rates relative to the Comparator QIV for all influenza strains (Table 7). Analyses of immunogenicity endpoints by gender did not demonstrate meaningful differences between males and females. The study population was not sufficiently diverse to assess differences between races or ethnicities.

Table 7: QIV-03: Post-Vaccination HI Antibody GMTs, Seroconversion Rates, and Analyses of Non-Inferiority of Afluria® Quad Vaccine Relative to Comparator QIV for each Strain 28 Days after Last Vaccination Among a Paediatric Population 6 months to < 5 Years of Age (Per Protocol Population)^a

Strain	Post-vaccination GMT		GMT Ratio ^b	Seroconversion % ^c		Difference Comparat or minus Afluria® Quad (95% CI)	Met both pre- defined non- inferiority criteria? ^e
	Afluria® Quad N=1456	Comparator N=484		Comparator over Afluria® Quad (95% CI)	Afluria® Quad N=1456 (95% CI)		
A/H1N1	353.3 (n=1455 ^f)	281.0 (n=484)	0.79 (0.72, 0.88)	79.1 (76.9, 81.1) (n=1456)	68.8 (64.5, 72.9) (n=484)	-10.3 (-15.4, - 5.1)	Yes
A/H3N2	393.0 (n=1454 th)	500.5 (n=484)	1.27 (1.15, 1.42)	82.3 (80.2, 84.2) (n=1455 ^h)	84.9 (81.4, 88.0) (n=484)	2.6 (-2.5, 7.8)	Yes
B/YAM	23.7 (n=1455 ^f)	26.5 (n=484)	1.12 (1.01, 1.24)	38.9 (36.4, 41.4) (n=1456)	41.9 (37.5, 46.5) (n=484)	3.1 (-2.1, 8.2)	Yes
B/VIC	54.6 (n=1455 ^f)	52.9 (n=483 ^g)	0.97 (0.86, 1.09)	60.2 (57.6, 62.7) (n=1456)	61.1 (56.6, 65.4) (n=483 ^g)	0.9 (-4.2, 6.1)	Yes

Abbreviations: Abbreviations: B/VIC, B Victoria lineage; B/YAM, B Yamagata lineage; CI, confidence interval; Comparator QIV, Fluzone® Quadrivalent QIV [Sanofi Aventis], GMT (adjusted), geometric mean titre.

^a The Per-Protocol Population comprised all subjects in the Evaluable Population who did not have any protocol deviations that were medically assessed as potentially impacting on immunogenicity results.

^b GMT Ratio = Comparator QIV / Afluria® Quad. Adjusted analysis model: Log-transformed Post-Vaccination HI Titre=Vaccine + Age Cohort [6 months to < 3 years or 3 to < 5 years] + Gender + Vaccination History [y/n] + Log-transformed Pre-Vaccination HI Titre + Site + Number of Doses (1 vs 2) + Age Cohort*Vaccine. The Age Cohort*Vaccine interaction term was excluded from the model fit for the strains B/Yamagata and B/Victoria as the interaction result was non-significant (p > 0.05). Least square means were back transformed.

^c Seroconversion rate was defined as the percentage of subjects with either a prevaccination HI titre < 1:10 and a postvaccination HI titre ≥ 1:40 or a prevaccination HI titre ≥ 1:10 and a 4-fold increase in postvaccination HI titre.

^d Seroconversion rate difference = Comparator QIV SCR percentage minus Afluria® Quad SCR percentage.

^e Noninferiority (NI) criterion for the GMT ratio: upper bound of two-sided 95% CI on the GMT ratio of Comparator QIV/ Afluria® Quad should not exceed 1.5. NI criterion for the SCR difference: upper bound of two sided 95% CI on the difference between SCR Comparator QIV – Afluria® Quad should not exceed 10%.

^f Subject 8400402-0073 was excluded from the Per-Protocol Population for the adjusted GMT analysis for the GMT ratio since the subject did not have information on all covariates (unknown prevaccination history).

^g Subject 8400427-0070 had a missing B/Victoria antigen pre-vaccination titre.

^h Subject 8400402-0074 had a missing A/H3N2 post-vaccination titre.

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Non-clinical studies have not been conducted with Afluria® Quad vaccine. A rat reproductive and developmental toxicity study has been conducted with Seqirus' trivalent influenza vaccine, Fluvax®. This study did not demonstrate any maternal or developmental toxicity.

Genotoxicity

Afluria® Quad / Afluria® Quad Junior vaccine has not been evaluated for genotoxic potential.

Carcinogenicity

Afluria® Quad / Afluria® Quad Junior vaccine has not been evaluated for carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Each dose also contains, nominally, the following excipients:

Excipient	Afluria® Quad Quantity per 0.5 mL dose	Afluria® Quad Junior Quantity per 0.25 mL dose
Sodium chloride	4.1 mg	2.05 mg
Dibasic sodium phosphate	0.3 mg	0.15 mg
Monobasic sodium phosphate	0.08 mg	0.04 mg
Potassium chloride	0.02 mg	0.01 mg
Monobasic potassium phosphate	0.02 mg	0.01 mg
Calcium chloride dihydrate	0.5 microgram	0.25 microgram
Water for injections	to 0.5 mL	to 0.25 mL

Afluria® Quad does not contain any antimicrobial preservative.

See also **Section 2 - QUALITATIVE AND QUANTITATIVE COMPOSITION.**

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 Afluria® Quad is 15 months from the date of manufacture.

The shelf life of Afluria® Quad Junior is 12 months from the date of manufacture. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2 °C to 8 °C (Refrigerate. Do not freeze). Protect from light. Discard if the vaccine has been frozen.

6.5 NATURE AND CONTENTS OF CONTAINER

Afluria® Quad inactivated quadrivalent influenza vaccine (split virion), 60 microgram HA, suspension for injection, is supplied in a single-dose 0.5 mL pre-filled needle free syringe (type 1 glass). Pack sizes: 1s; 10s.

Afluria® Quad inactivated quadrivalent influenza vaccine (split virion), 60 microgram HA, suspension for injection, is also supplied in a single-dose 0.5 mL pre-filled syringe (type 1 glass) with attached needle for injection. Pack sizes: 1s; 10s.

Afluria® Quad Junior inactivated quadrivalent influenza vaccine (split virion), 30 microgram HA, suspension for injection, is supplied in a single-dose 0.25 mL pre-filled needle free syringe (type 1 glass). Pack sizes: 1s; 10s.

Afluria® Quad Junior inactivated quadrivalent influenza vaccine (split virion), 30 microgram HA, suspension for injection, is also supplied in a single-dose 0.25 mL pre-filled syringe (type 1 glass) with attached needle for injection. Pack sizes: 1s; 10s.

The syringe and all associated syringe components for Afluria® Quad and Afluria® Quad Junior do not contain natural rubber latex.

Not all presentations or pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Afluria® Quad / Afluria® Quad Junior vaccine is presented as a single-use syringe and any remaining contents should be discarded in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Seqirus (NZ) Ltd

PO Box 62590

Greenlane

Auckland 1546

NEW ZEALAND

Telephone: 0800 502 757

9 DATE OF FIRST APPROVAL

Afluria® Quad: 12 October 2017

Afluria® Quad Junior: 19 December 2019

10 DATE OF REVISION OF THE TEXT

27 October 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
1 Product Name	Tradename of new strength presentation added.
2 Qualitative and Quantitative Composition	Information related to composition of new strength added. Update to list of excipients/trace amounts.
4.1 Therapeutic Indications	Revision of current indication of 5 years and older to 3 years and older. New indication for use in children 6 months and older.
4.2 Dose and method of administration	Dosing information added for use in children 6 months and older. Revision of age group of 5 years to < 9 years to: 3 years to < 9 years.
4.3 Contraindications	Contraindications updated to exclude egg protein
4.4 Special warnings and precautions for use	Precautions for use in children, persons with egg anaphylaxis and persons with febrile illness added.
4.8 Undesirable effects	Adverse effects updated with paediatric trial outcomes.
5.1 Pharmacodynamic properties	Pharmacodynamic effects updated to reflect current recommendations. Clinical trial data updated with paediatric trial outcomes.
6.5 Nature and contents of container	Description of new strength and presentation added.
2. Qualitative and Quantitative Composition	Influenza strains and season year updated for Southern Hemisphere 2020. Addition of TDOC specification and manufacturing residue hydrocortisone.
6. 1 List of excipients	Excipients listed in table format
6.3	Update to text to clarify the shelf life of both products in this datasheet.
2	Influenza strains and season year updated for Southern Hemisphere 2021 season. Revision of quantities of TDOC & Ovalbumin.
4.2	Dose and method of administration updated to include to ‘use in one patient on one occasion only and discard any residue’.
4.8	Post marketing section of Adverse effects updated.
4.6, 4.8, 5.3	Sections updated to delete ‘TIV’.
6.1	Section updated with preservative statement.

Section Changed	Summary of new information
6.4	Storage condition revised to align with Company core data sheet and special precautions for use updated with advice to discard the vaccine if frozen.
	Revision of trademark attribution statement
2	Influenza strains and season year updated for Southern Hemisphere 2022 season.

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