1128943

For Use of Registered Medical Practitioner or a Hospital or a Laboratory Only

Inactivated Influenza Vaccine (Surface Antigen) I.P. (Quadrivalent)

INFLUVAC® TETRA *2021/2022* (Suspension for injection)

COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains*:

A/Victoria/2570/2019 (H1N1)pdm09-like strain (A/Victoria/2570/2019, IVR-215)	15 µg HA**
A/Cambodia/e0826360/2020 (H3N2)-like strain (A/Cambodia/e0826360/2020, IVR-224)	15 µg HA**
B/Washington/02/2019-like strain (B/Washington/02/2019, wild type)	15 µg HA**
B/Phuket/3073/2013-like strain (B/Phuket/3073/2013, wild type)	15 µg HA** per 0.5 ml dose

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

This vaccine complies with the World Health Organization (WHO) recommendation (northern hemisphere) and competent authority decision for the 2021/2022 season.

Influvac® Tetra may contain traces of eggs (such as ovalbumin, chicken proteins), formaldehyde, cetyltrimethylammonium bromide, polysorbate 80 or gentamicin, which are used during the manufacturing process.

PHARMACEUTICAL FORM

Suspension for injection in prefilled syringes;
A colourless clear liquid, filled in single-dose syringes (glass, type I).

CLINICAL PARTICULARS

Therapeutic indications

Prophylaxis of influenza, especially those who run an increased risk of associated complications. Influvac® Tetra is indicated in adults (18 years of age or older) and children from 6 months of age. The use of Influvac® Tetra should be based on official recommendations.

Posology and method of administration

Posology Adults: 0.5 ml.

Paediatric population

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

Method of Administration

Immunisation should be carried out by intramuscular injection.
Precautions to be taken before handling or administrating the medicinal product:
For instructions for preparation of the medicinal product before administration, see section **'Special precautions for disposal and other handling'**

Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in 'List of excipients' or to any component that may be present as traces such as eggs (ovalbumin, chicken proteins), formaldehyde, cetyltrimethylammonium bromide, polysorbate 80 or gentamicin.

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

Special warnings and precautions for use

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.

Influvac® Tetra should under no circumstances be administered intravascularly.

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

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

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium free'. This medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially "potassium- free".

Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. If Influvac® Tetra is given at the same time as other vaccines, immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique disproves the false-positive ELISA test results. The transient false-positive reactions could be due to the IgM response by the vaccine.

Fertility, pregnancy and lactation

Pregnancy

Inactivated influenza vaccines can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester; however, data from worldwide use of influenza vaccine do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

Breastfeeding

Influvac® Tetra may be used during breastfeeding.

Fertility

No fertility data are available

Effects on ability to drive and use machines

Influvac® Tetra has no or negligible influence on the ability to drive and use machines.

Undesirable effects

a. Summary of the safety profile

The safety of Influvac® Tetra was assessed in four clinical trials, two global and two Indian trials. In the global clinical trials, healthy adults 18 years of age and older, and healthy children 3 to 17 years of age were administered Influvac® Tetra or trivalent influenza vaccine Influvac®. Children from 3 to 8 years of age received one or two doses of Influvac® Tetra depending on their influenza vaccination history.

In the Indian clinical trials, healthy adults 18 years of age and older, were administered Influvac® Tetra or a reference vaccine (marketed quadrivalent inactivated influenza vaccine) and healthy children 6 months to 17 years of age were administered Influvac® Tetra. Children from 6 months to 8 years of age received one or two doses of Influvac® Tetra depending on their influenza vaccination history.

Most reactions usually occurred within the first 3 days following vaccination and resolved spontaneously within 1 to 3 days after onset. The intensity of these reactions was generally mild.

In all age groups, the most frequently reported local adverse reaction after vaccination observed in the clinical studies for Influvac® Tetra was vaccination site pain.

The most frequently reported general adverse reactions after vaccination observed in the clinical studies for Influvac® Tetra in adults and children from 6 – 17 years of age were fatigue and headache, for children from 3 – 5 years of age drowsiness, irritability and loss of appetite.,

Similar rates of solicited adverse reactions were observed in recipients of Influvac® Tetra and trivalent influenza vaccine Influvac®.

b. Tabulated summary of adverse reactions

Global Data-Clinical trials and post-marketing experience:

The following undesirable effects are considered at least possibly related to Influvac® Tetra and have either been observed during the clinical trials with Influvac® Tetra or are resulting from post-marketing experience with the trivalent influenza vaccine Influvac®.

The following frequencies apply:
very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); and not known (adverse reactions from post-marketing experience; cannot be estimated from the available data).

Adults and elderly

Adverse Reactions Reported with Influvac® Tetra/Influvac®				
MedDRA System Organ Class	**Very common ≥ 1/10**	**Common ≥ 1/100 to < 1/10**	**Uncommon ≥ 1/1,000 to < 1/100**	**Not Known[a] (cannot be estimated from the available data)**
Blood and lymphatic system				Transient thrombocytopenia, transient lymphadenopathy
Immune system disorders				Allergic reactions, in rare cases leading to shock, angioedema
Nervous system disorders	Headache[b]			Neuralgia, paraesthesia, febrile convulsions, neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome
Vascular disorders				Vasculitis associated in very rare cases with transient renal involvement
Skin and subcutaneous tissue disorders		Sweating		Generalised skin reactions including pruritus, urticaria or non-specific rash
Musculoskeletal and connective tissue disorders		Myalgia Arthralgia		
General disorders and administration site conditions	Fatigue Local reaction: pain	Malaise, shivering Local reactions: redness, swelling, ecchymosis, induration	Fever	

[a] Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
[b] In elderly adults (≥ 61 years) reported as common

Paediatric population

Children (3 to 17 years of age) -Adverse Reactions Reported with Influvac® Tetra/Influvac®				
MedDRA System Organ Class	**Very common ≥ 1/10**	**Common ≥ 1/100 to < 1/10**	**Uncommon ≥ 1/1,000 to < 1/100**	**Not Known[a] (cannot be estimated from the available data)**
Blood and lymphatic system				Transient thrombocytopenia, transient lymphadenopathy
Immune system disorders				Allergic reactions, in rare cases leading to shock, angioedema
Nervous system disorders	Headache,[d] Drowsiness[b]			Neuralgia, paraesthesia, febrile convulsions, neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome
Vascular disorders				Vasculitis associated in very rare cases with transient renal involvement
Skin and subcutaneous tissue disorders		Sweating[c]		Generalised skin reactions including pruritus, urticaria or non-specific rash
Metabolism and nutrition disorders	Appetite loss[b]			
Gastrointestinal disorders	Gastrointestinal symptoms[d]	Diarrhoea[b], vomiting[b]		
Psychiatric disorders	Irritability[b]			
Musculoskeletal and connective tissue disorders	Myalgia[d]	Arthralgia[d]		
General disorders and administration site conditions	Fatigue[d], malaise[d] Local reactions: pain[c], redness[c], swelling[c], induration[c]	Fever[c], shivering[d] Local reaction: ecchymosis[c]		

[a] Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure
[b] Reported as a solicited symptom in children 3 to 5 years of age
[c] Reported as a solicited symptom in children 3 to 17 years of age
[d] Reported as a solicited symptom in children 6 to 17 years of age

Indian Data-Clinical Trials:
In a clinical trial (INFQ3005), healthy adults and elderly subjects were administered Influvac® Tetra or a reference vaccine (marketed quadrivalent inactivated influenza vaccine). Fever and headache were commonly reported systemic reactions and vaccination site pain was commonly reported as a local reaction.

In a clinical trial (INFQ3004), children and adolescents 6 months to 17 years of age were administered Influvac® Tetra. Children from 6 months to 8 years of age received one or two doses of Influvac® Tetra depending on their influenza vaccination history.

In 6 to 35 months of age group, fever, irritability/fussiness drowsiness, diarrhea/vomiting, and loss of appetite were commonly reported systemic reactions within 7 days after vaccination. Vaccination site pain was reported very commonly as a local reaction.

In 3 to 17 years of age group, fever was commonly reported systemic reactions within 7 days after vaccination. Other commonly reported systemic reactions included headache, fatigue/ tiredness and malaise. Vaccination site pain was reported very commonly as a local reaction.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to webmasterindia@abbott.com

Overdose
Overdosage is unlikely to have any untoward effect.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Influenza vaccine, ATC Code: J07BB02.

Mechanism of action:
Influvac® Tetra provides active immunisation against four influenza virus strains: an A/(H1N1) strain, an A/(H3N2) strain, and two B strains (one from each lineage; B/(Victoria) and B/(Yamagata)). Influvac® Tetra manufactured according to the same process as trivalent influenza vaccine Influvac®, induces humoral antibodies against the haemagglutinins. These antibodies neutralise influenza viruses. Specific levels of hemagglutination-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.

An immune response is generally obtained within 2 to 3 weeks. The duration of post-vaccinal immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6-12 months.

Pharmacodynamic effects:
Data from Global Clinical Trials:

Immunogenicity of Influvac® Tetra compared to trivalent Influvac®:
Clinical studies performed in adults of 18 years of age and older (INFQ3001) and children and adolescents 3 years - 17 years of age (INFQ3002) assessed the safety and immunogenicity of Influvac® Tetra and its non-inferiority to trivalent influenza vaccine Influvac® for the post vaccination HI Geometric mean antibody titer (GMT).
In both studies the immune response elicited by Influvac® Tetra against the three strains in common was non-inferior to trivalent influenza vaccine Influvac®. Influvac® Tetra elicited a superior immune response against the additional B strain included in Influvac® Tetra compared to trivalent influenza vaccine Influvac®.

Adults 18 years of age and older:
In clinical study INFQ3001, 1,535 adults of 18 years of age and older received a single dose of Influvac® Tetra and 442 subjects received a single dose of trivalent Influvac:

Table: Post-vaccination GMT

Adults 18 – 60 years of age	Influvac® Tetra N=768	Influvac® [1] N=112	Influvac® [2] N=110
	GMT (95% confidence interval)		
A/H1N1	272.2 (248.0 , 298.8)	304.4 (235.1 , 394.1)	316.0 (245.1 , 407.3)
A/H3N2	442.4 (407.6 , 480.2)	536.5 (421.7 , 682.6)	417.0 (323.7 , 537.1)
B (Yamagata)[3]	162.5 (147.8 , 178.7)	128.7 (100.3 , 165.2)	81.7 (60.7 , 109.9)
B (Victoria)[4]	214.0 (195.5 , 234.3)	85.1 (62.6 , 115.6)	184.7 (139.0 , 245.3)

Elderly 61 years of age and older	Influvac® Tetra N=765	Influvac® [1] N=108	Influvac® [2] N=110
	GMT (95% confidence interval)		
A/H1N1	127.2 (114.9 , 140.9)	142.4 (107.6 , 188.3)	174.2 (135.9 , 223.3)
A/H3N2	348.5 (316.8 , 383.5)	361.5 (278.3 , 469.6)	353.4 (280.7 , 445.0)
B (Yamagata)[3]	63.7 (57.7 , 70.4)	57.4 (43.6 , 75.7)	27.3 (20.7 , 36.0)
B (Victoria)[4]	109.4 (98.1 , 122.0)	48.0 (34.6 , 66.6)	106.6 (79.7 , 142.8)

N= number of subjects included in efficacy analysis
[1] containing A/H1N1, A/H3N2 and B (Yamagata lineage)
[2] containing A/H1N1, A/H3N2 and B (Victoria lineage)
[3] recommended B strain by WHO for the season 2014-2015 NH for trivalent vaccines
[4] additional recommended B strain by WHO for season 2014-2015 NH for quadrivalent vaccines

Paediatric population
Children 3 - 17 years of age:
In clinical study INFQ3002, 402 children of 3 to 17 years of age received one or two doses of Influvac® Tetra and 798 children received one or two doses of trivalent Influvac® based on their influenza vaccination history.

Table: Post-vaccination GMT

Children 3 - 17 years of age	Influvac® Tetra N=396	Influvac® [1] N=389	Influvac® [2] N=399
	GMT (95% confidence interval		
A/H1N1	546.2 (487.1 , 612.6)	605.6 (536.3 , 83.8)	633.1 (562.8 , 712.2)
A/H3N2	1161.5 (1035.8 , 1302.5)	1075.4 (947.7 , 1220.3)	1306.4 (1162.5, 1468.1)
B (Yamagata)[3]	280.8 (246.2 , 320.1)	269.0 (232.8 , 310.7)	38.3 (31.9 , 46.1)
B (Victoria)[4]	306.7 (266.0 , 353.6)	104.5 (86.8 , 125.8)	361.4 (311.0 , 420.0)

N= number of subjects included in efficacy analysis
[1] containing A/H1N1, A/H3N2 and B (Yamagata lineage)
[2] containing A/H1N1, A/H3N2 and B (Victoria lineage)
[3] recommended B strain by WHO for the season 2016-2017 NH for trivalent vaccines
[4] additional recommended B strain by WHO for season 2016-2017 NH for quadrivalent vaccines

Data from Indian Clinical Trials:

A clinical study performed in healthy adult and elderly subjects (INFQ3005) assessed the safety and immunogenicity of Influvac® Tetra and its non-inferiority to a quadrivalent influenza vaccine for the post vaccination HI Geometric mean antibody titer (GMT). The study demonstrated that Influvac® Tetra elicited an adequate immune response.

Adults aged 18-60 years:
In INFQ3005, 118 subjects received Influvac® Tetra and 121 subjects received Reference vaccine (inactivated quadrivalent influenza vaccine).

Table: Post-vaccination GMT

Adults 18 – 60 years of age	Influvac® Tetra N=118	Reference vaccine N=121
	GMT (95% confidence interval)	
A/H1N1	492.1 (371.1, 652.4)	457.8 (350.8, 597.3)
A/H3N2	766.7 (583.4, 1007.6)	781.0 (642.8, 948.8)
B (Yamagata)	31.0 (22.5, 42.7)	30.3 (22.0, 41.6)
B (Victoria)	32.8 (23.0, 46.8)	43.4 (30.9, 60.9)

N= number of subjects included in efficacy analysis

Elderly 61 years of age and older:
In INFQ3005, 118 subjects received Influvac® Tetra and 116 subjects received reference vaccine (inactivated quadrivalent influenza vaccine).

Table: Post-vaccination GMT

Elderly 61 years of age and older	Influvac® Tetra N=118	Reference vaccine N=116
	GMT (95% confidence interval)	
A/H1N1	414.4 (296.9, 578.4)	340.2 (248.5, 465.8)
A/H3N2	705.1 (518.3, 959.3)	916.0 (729.4, 1150.3)
B (Yamagata)	22.5 (16.2, 31.2)	23.9 (17.1, 33.2)
B (Victoria)	30.6 (21.0, 44.6)	39.3 (27.3, 56.6)

N= number of subjects included in efficacy analysis

A clinical study performed in children and adolescents 6 months - 17 years of age (INFQ3004) assessed the safety and immunogenicity of Influvac® Tetra for the post vaccination HI Geometric mean antibody titer (GMT). The study demonstrated that Influvac® Tetra elicited an adequate immune response.

Children 6 to 35 months of age:
In clinical study INFQ3004, 114 children of 6 to 35 months of age received one or two doses of Influvac® Tetra based on their influenza vaccination history.

Table: Post-vaccination GMT

Children 6 to 35 months of age	Influvac® Tetra N=114 (Full Analysis Sample)
GMT (95% confidence interval	
A/H1N1	196.7 (134.4 ,287.9)
A/H3N2	301.6 (216.0 ,421.0)
B (Yamagata)	50.6 (37.0 ,69.3)
B (Victoria)	22.4 (15.8 ,31.7)

N= number of subjects included in efficacy analysis

Children/adolescents 3 to 17 years of age:
In clinical study INFQ3004, 118 children/adolescents 3 to 17 years of age received Influvac® Tetra. Children from 6 months to 8 years of age received one or two doses of Influvac® Tetra depending on their influenza vaccination history.

Table: Post-vaccination GMT

Children/adolescents 3 to 17 years of age	Influvac® Tetra N=118 (Full Analysis Sample)
GMT (95% confidence interval	
A/H1N1	915.8 (680.6 ,1232.3)
A/H3N2	1576.8 (1284.0 ,1936.4)
B (Yamagata)[3]	149.5 (115.2 ,194.2)
B (Victoria)[4]	94.4 (66.8 ,133.5)

N= number of subjects included in efficacy analysis

Pharmacokinetic properties
Not applicable.

Preclinical safety data
Non-clinical data revealed no special hazard for humans based on conventional studies of repeat dose and local toxicity, reproductive and developmental toxicity and safety pharmacology studies.

PHARMACEUTICAL PARTICULARS
List of excipients
Potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, sodium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate and water for injections.

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

Shelf-life
1 year.

Special precautions for storage Store in a refrigerator (+2°C to +8°C). Do not freeze.
Store in the original package in order to protect from light.

Nature and contents of the container
0.5 ml suspension for injection in prefilled syringe with needle (glass, type I), pack of 1

Special precautions for disposal and other handling
The vaccine should be allowed to reach room temperature before use. Shake before use. Inspect visually prior to administration.

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

MANUFACTURED BY:
Abbott Biologicals B.V.
Veerweg 12, 8121AA Olst
The Netherlands

IMPORTED AND MARKETED BY:
Abbott India Limited
Cold Room No. 601,
Plot No. K-12,
M.I.D.C, Taloja, Panvel
Tal: Panvel (Raigad)
Pin: 410208, India

DATE OF APPROVAL/REVISION OF THIS TEXT
April 2021

Abbott
1128943