

เอกสารกำกับยาภาษาอังกฤษ
INFLUVAC® Tetra 2021
Influenza vaccine SH2021

1. NAME OF THE MEDICINAL PRODUCT

INFLUVAC® Tetra, suspension for injection in pre-filled syringe
Influenza vaccine (surface antigen, inactivated).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

- A/Victoria/2570/2019 (H1N1)pdm09-like strain (A/Victoria/2570/2019, IVR-215)	15 micrograms HA **
- A/Hong Kong/2671/2019 (H3N2)-like strain (A/Hong Kong/2671/2019, IVR-208)	15 micrograms HA **
- B/Washington/02/2019-like strain (B/Washington/02/2019, wild type)	15 micrograms HA **
- B/Phuket/3073/2013-like strain (B/Phuket/3073/2013, wild type)	15 micrograms HA **

per 0.5 ml dose.

* propagated in fertilised hens' eggs from healthy chicken flocks

** haemagglutinin.

This vaccine complies with the World Health Organisation (WHO) recommendation (southern hemisphere) and competent authority decision for the 2021 season.

For a full list of excipients see section 6.1.

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 (see section 4.3).

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe;
colourless clear liquid, filled in single-dose syringes.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of influenza; especially those who run an increased risk of associated complications.

INFLUVAC® Tetra is indicated in adults and children from 3 years of age

The use of INFLUVAC® Tetra should be based on official recommendations.

Vaccination is particularly recommended for the following categories of patients, depending on national immunization policies:

- Persons aged ≥ 65 years, regardless their health condition.
- Adults and children from 3 years of age with chronic disorders of the pulmonary or cardiovascular systems, including asthma.
- Adults and children from 3 years of age with chronic metabolic diseases such as diabetes mellitus.
- Adults and children from 3 years of age with chronic renal dysfunction.
- Adults and children from 3 years of age with immunodeficiencies due to disease or immunosuppressant medication (e.g., cytostatics or corticosteroids) or radiotherapy.
- Children from 3 years of age who receive long-term acetylsalicylic acid containing medication and might therefore be at risk for developing Reye's syndrome following an influenza infection.

4.2 Posology and method of administration

Posology

Adults: 0.5 ml.

Paediatric population

Children from 3 to 17 years 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.

Children less than 3 years of age: the safety and efficacy of INFLUVAC[®] Tetra in children have not been established.

Method of Administration

Immunisation should be carried out by intramuscular or deep subcutaneous injection.

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

For instructions for preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1 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.

4.4 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.

As with other vaccines administered intramuscularly, INFLUVAC[®] Tetra should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

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.

INFLUVAC[®] Tetra is not effective against all possible strains of influenza virus. INFLUVAC[®] Tetra is intended to provide protection against those strains of virus from which the vaccine is prepared and to closely related strains.

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

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

Interference with serological testing: see section 4.5.

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”.

4.5 Interactions 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.

4.6 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.

Breast-feeding

INFLUVAC[®] Tetra may be used during breast-feeding.

Fertility

No fertility data are available.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

a. Summary of the safety profile

The safety of INFLUVAC[®] Tetra was assessed in two clinical trials in which 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 Influxac. Children from 3 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 Influxac.

b. Tabulated summary of adverse reactions

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

The following frequencies apply:

very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1,000$, $< 1/100$); and not known (adverse reactions from post-marketing experience; cannot be estimated from the available data).

Adult and elderly:

Adverse Reactions Reported with INFLUVAC [®] Tetra / Influxac				
MedDRA System Organ Class	Very common $\geq 1/10$	Common $\geq 1/100$ to $< 1/10$	Uncommon $\geq 1/1,000$ 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

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)
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	
<p>^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.</p> <p>^b In elderly adults (≥ 61 years) reported as common</p>				

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		
<p>^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</p> <p>^b Reported as a solicited symptom in children 3 to 5 years of age</p> <p>^c Reported as a solicited symptom in children 3 to 17 years of age</p> <p>^d Reported as a solicited symptom in children 6 to 17 years of age</p>				

4.9 Overdose

Overdosage is unlikely to have any untoward effect.

5. PHARMACOLOGICAL PROPERTIES

5.1 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 the 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 postvaccinal immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6-12 months.

Pharmacodynamic effects:

Immunogenicity of INFLUVAC[®] Tetra compared to trivalent influenza vaccine Influvac:

Clinical studies performed in adults of 18 years of age and older (INFQ3001) and children of 3 to 17 years of age (INFQ3002) assessed the safety and immunogenicity of INFLUVAC[®] Tetra and its non-inferiority to trivalent influenza vaccine Influvac for the postvaccination 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	Influvac¹ N=112	Influvac² 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	Influvac¹ N=108	Influvac² 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

¹containing A/H1N1, A/H3N2 and B (Yamagata lineage)

²containing A/H1N1, A/H3N2 and B (Victoria lineage)

³recommended B strain by WHO for the season 2014-2015 NH for trivalent vaccines

⁴additional 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	<i>INFLUVAC[®] Tetra</i> 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

¹containing A/H1N1, A/H3N2 and B (Yamagata lineage)

²containing A/H1N1, A/H3N2 and B (Victoria lineage)

³recommended B strain by WHO for the season 2016-2017 NH for trivalent vaccines

⁴additional recommended B strain by WHO for season 2016-2017 NH for quadrivalent vaccines

5.2 Pharmacokinetic properties

Not applicable.

5.3 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, sodium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate and water for injections.

6.2 Incompatibilities

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

6.3 Shelf life

1 year

6.4 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.

6.5 Nature and contents of container

0.5 ml suspension for injection in pre-filled syringe with or without needle (glass, type I), pack of 1 syringe.

6.6 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.

7. MARKETING AUTHORISATION HOLDER

Manufactured by:

Abbott Biologicals B.V.
C.J. van Houtenlaan 36
NL-1381 CP Weesp
The Netherlands

Packed and released by:

Abbott Biologicals B.V.
Veerweg 12
NL-8121 AA Olst
The Netherlands

Imported by:

Abbott Laboratories Ltd.,
Bangkok, Thailand

8. MARKETING AUTHORISATION NUMBER(S)

2C 6/62 (NBC)

9. DATE OF AUTHORISATION

August 2019

10. DATE OF REVISION OF THE TEXT

December 2020

(RDCCDS000649/7)