SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TicoVac Junior 0.25 ml, Suspension for injection in a pre-filled syringe
Tick-Borne Encephalitis Vaccine (whole virus, inactivated)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.25 ml) contains:

Tick-Borne Encephalitis Virus[1,2] (strain Neudörfl) 1.2 micrograms
[1]adsorbed on aluminium hydroxide, hydrated (0.17 milligrams Al^{3+})
[2]produced in chick embryo fibroblast cells (CEF cells)

Excipient(s) with known effect
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in a pre-filled syringe.
After shaking the vaccine is an off-white, homogenous, opalescent suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TicoVac Junior 0.25 ml is indicated for the active (prophylactic) immunization of children aged from 1 year to 15 years against tick-borne encephalitis (TBE).

TicoVac Junior 0.25 ml is to be given on the basis of official recommendations regarding the need for, and timing of, vaccination against TBE.

4.2 Posology and method of administration

Posology

Primary vaccination schedule
The primary vaccination schedule is the same for all persons from 1 year to 15 years of age and consists of three doses of TicoVac Junior 0.25 ml.
The first and second dose should be given at a 1 to 3 month interval.
If there is a need to achieve an immune response rapidly, the second dose may be given two weeks after the first dose. After the first two doses a sufficient protection for the ongoing tick season is to be expected (see section 5.1).
The third dose should be given 5 to 12 months after the second vaccination. After the third dose protection is expected to last for at least 3 years.

To achieve immunity before the beginning of the seasonal tick activity, which is in spring, the first and second doses should preferably be given in the winter months. The vaccination schedule should ideally be completed

with the third vaccination within the same tick season or at the least before the start of the following tick season.

Basic Immunization	Dose	Conventional Schedule	Rapid Immunization Schedule
1st dose	0.25 ml	Elected date	Elected date
2nd dose	0.25 ml	1 to 3 months after the 1st vaccination	14 days after the 1st vaccination
3rd dose	0.25 ml	5 to 12 months after the 2nd vaccination	5 to 12 months after the 2nd vaccination

Booster doses
The first booster dose should be given 3 years after the third dose (see section 5.1).
Sequential booster doses should be given every 5 years after the last booster dose.

Booster dose	Dose	Timing
1st booster	0.25 ml	3 years after the 3rd vaccination
Sequential booster doses	0.25 ml	every 5 years

Extending the interval between any of the doses (primary vaccination schedule and booster doses) may leave subjects with inadequate protection against infection (see section 5.1).
However, in the case of an interrupted vaccination schedule of at least two previous vaccinations, a single catch-up dose is sufficient to continue the vaccination schedule (see section 5.1).

No data regarding catch-up dose in children less than 6 years of age are available (see section 5.1).

Children with an impaired immune system (including those undergoing immunosuppressive therapy)
There are no specific clinical data on which to base dose recommendations. However, consideration may be given to determining the antibody concentration at four weeks after the second dose and administering an additional dose if there is no evidence of seroconversion at this time. The same applies to any of the following doses.

Method of administration

The vaccine should be given by intramuscular injection into the upper arm (deltoid muscle).

In children up to 18 months of age, or dependent on a child's development and nutrition status, the vaccine is administered into the thigh muscle (vastus lateralis muscle).

In exceptional cases only (in subjects with a bleeding disorder or in subjects receiving prophylactic anticoagulation), the vaccine may be administered subcutaneously (see sections 4.4 and 4.8).

Care must be taken to avoid accidental intravascular administration (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 Cross allergies with aminoglycosides other than neomycin and gentamycin should be considered.
Severe hypersensitivity to egg and chick proteins (anaphylactic reaction after oral ingestion of egg protein) may cause severe allergic reactions in sensitized individuals (see also section 4.4).
TBE vaccination should be postponed if the person is suffering from a moderate or severe acute illness (with or without fever).

4.4 Special warnings and precautions for use

As with all vaccines that are administered by injection, appropriate emergency treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.
Non-severe allergy to egg protein does not usually constitute a contraindication to vaccination with TicoVac Junior 0.25 ml. Nevertheless, such persons should only be vaccinated under appropriate supervision and facilities for emergency management of hypersensitivity reactions should be available.

The levels of potassium and sodium are at less than 1 mmol per dose, i.e., essentially “potassium and sodium-free”.

Intravascular administration must be avoided as this might lead to severe reactions, including hypersensitivity reactions with shock.

The recommended route of administration is intramuscular. However, this may not be appropriate in subjects with a bleeding disorder or subjects receiving prophylactic anticoagulation. Limited data in healthy adults suggest comparable immune response for subcutaneous booster vaccinations when compared to intramuscular booster vaccinations. However, subcutaneous administration might lead to an increased risk for local adverse reactions. No data are available for children/adolescents. Furthermore, no data are available for primary immunisation via the subcutaneous route.

Fever may occur in children after the first immunization in particular in the very young (see section 4.8). In general, the fever subsides within 24 hours. Fever rates reported after the second vaccination are generally lower as compared to the fever rates after the first vaccination. In children with a history of fever convulsions or high fever following vaccinations, antipyretic prophylaxis or treatment may be considered.

A protective immune response may not be elicited in persons undergoing immunosuppressive therapy.
Whenever serological testing is considered necessary in order to determine the need for sequential doses, assays should be performed in an experienced, qualified laboratory. This is because cross reactivity with pre-existing antibodies due to natural exposure or previous vaccination against other flaviviruses (e.g. Japanese encephalitis, Yellow fever, Dengue virus) may give false positive results.

In case of a known or suspected auto-immune disease in the intended recipient, the risk of TBE infection must be weighed against the risk that TicoVac Junior 0.25 ml might have an adverse effect on the course of the auto-immune disease.

Caution is required when considering the need for vaccination in children with pre-existing cerebral disorders such as active demyelinating disorders or poorly controlled epilepsy.
There is no data concerning post exposure prophylaxis with TicoVac Junior 0.25 ml.
As with all vaccines, TicoVac Junior 0.25 ml may not completely protect all vaccinees against the infection that it is intended to prevent. For details on product administration in persons with impaired immune system and persons undergoing immunosuppressive therapy please see section 4.2.

Tick bites may transmit infections other than TBE, including certain pathogens that can sometimes cause a clinical picture that resembles tick-borne encephalitis. TBE vaccines do not provide protection against Borrelia infection. Therefore, the appearance of clinical signs and symptoms of possible TBE infections in a vaccinee should be thoroughly investigated for the possibility of alternative causes.

4.5 Interactions with other medicinal products and other forms of interaction

No interaction studies with other vaccines or medicinal products have been performed. The administration of other vaccines at the same time as TicoVac Junior 0.25 ml should be performed only in accordance with official recommendations. If other injectable vaccines are to be given at the same time, administrations should be into separate sites and, preferably, into separate limbs.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data from the use of TicoVac Junior 0.25 ml in pregnant women.

Breast-feeding
It is unknown whether TicoVac Junior 0.25 ml is excreted in human milk.
Therefore, TicoVac Junior 0.25 ml should only be administered during pregnancy and to breastfeeding women when it is considered urgent to achieve protection against TBE infection and after careful consideration of the risk-benefit relationship.

4.7 Effects on the ability to drive and to use machines

TicoVac Junior 0.25 ml is unlikely to affect a child's motor skills (e.g., when playing in the street or cycling) or ability to use machines. It should be taken into account, however, that impaired vision or dizziness may occur.

4.8 Undesirable effects

The calculated frequencies are based on a pooled analysis of adverse reactions reported after the 1st vaccination (3088 subjects) from 8 clinical studies conducted with TicoVac Junior 0.25 ml (1.2 µg) in subjects aged 1-15 years of age. Rates of systemic adverse reactions observed after the 2nd and 3rd vaccination were lower than after the 1st vaccination. Comparable rates of injection site reactions are observed after the first, second and third vaccination.

The following other undesirable effects listed in this Section are given according to the recommended frequency convention:

Adverse Reactions from clinical trials

System organ class	Frequency			
	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)**
Blood and lymphatic system disorders			Lymphadenopathy	
Metabolism and nutrition disorders		Decreased Appetite		
Psychiatric disorders		Restlessness[1], Sleeping disorder		
Nervous system disorders		Headache		Sensory abnormalities, Dizziness
Ear and labyrinth disorders				Vertigo
Gastrointestinal disorders		Nausea, Vomiting	Abdominal pain	Diarrhoea, Dyspepsia
Skin and subcutaneous tissue disorders				Urticaria
Musculoskeletal and connective tissue disorders		Myalgia	Arthralgia	

[1] Frequency is estimated based on data from children aged 1-5 years

General disorders and administration site conditions	Injection site reactions[2] e.g., Injection site pain	Pyrexia[3], Fatigue, Malaise[4] Injection site reactions such as • Swelling • Induration • Erythema	Chills	Injection site pruritus

Fever was measured rectally in children up to at least 3 years of age and orally in children 3 years of age and older. The analysis includes any fever temporally associated with vaccination whether or not causally related.

Fever is age dependent and is decreasing with the number of vaccinations.
In a safety study and dose finding studies the fever rates observed after the first vaccination were as follows: 1 to 2 year olds (n=262): mild fever (38-39°C) in 27.9%; moderate fever (39.1-40.0°C) in 3.4%; no severe fever (>40°C). 3 to 15 year olds (n=2519): mild fever in 6.8%; moderate fever in 0.6%; no severe fever (>40°C).

Fever rates reported after the second vaccination are generally lower as compared to the fever rates after the first vaccination: 15.6% (41/263) in 1 to 2 year old children and 1.9% (49/2522) in 3 to 15 year old children.

Adverse reactions from post-marketing surveillance

The following additional adverse reactions have been reported in post-marketing experience.

System organ class	Frequency*
	Rare (≥1/10,000 to <1/1,000)
Immune system disorders	Anaphylactic reaction, hypersensitivity
Nervous system disorders	Encephalitis, convulsion (including febrile), meningism, polyneuropathy, motor dysfunction (hemiparesis/hemiplegia facial paresis, paralysis/paresis, neuritis), Guillain-Barré syndrome
Eye disorders	Visual impairment, photophobia, eye pain
Ear and labyrinth disorders	Tinnitus
Respiratory, thoracic and mediastinal disorders	Dyspnea
Skin and subcutaneous tissue disorders	Rash (erythematous, maculopapular, vesicular), erythema, pruritus, hyperhidrosis
Musculoskeletal and connective tissue disorders	Neck pain, musculoskeletal stiffness (including neck stiffness), pain in extremity
General disorders and administration site conditions	Gait disturbance, influenza-like illness, asthenia, edema

* The upper limit of the 95% confidence interval of the event frequency is calculated with 3/n, with n representing the number of subjects included in all clinical trials with TicoVac Junior 0.25 ml. Therefore, the calculated frequency "rare" represents the theoretical maximum frequency for these events

[2] A subject may have experienced more than 1 event.
[3] Fevers occurred more frequently in younger than in older children (i.e., Very common to Common, respectively). Fever rates after the second and third vaccinations are generally lower than after the first vaccination.
[4] Frequency is estimated based on data from children aged 6 – 15 years.

In a small comparative study on the immune response after intramuscular and subcutaneous administration of Ticovac in healthy adults, the subcutaneous route led to a higher local reactogenicity profile, particularly in women. No data are available in children.

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/.

4.9 Overdose

There are reports of children receiving the adult formulation. It is conceivable that the risk of adverse reactions is increased in such cases.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: encephalitis vaccines, ATC Code: J07 BA01

The pharmacodynamic effect of the product consists of the induction of a sufficiently high concentration of anti-TBE antibody to provide protection against the TBE virus.

The protection rate of the previous generation and current TBE vaccine has been determined during a continuous surveillance as performed among the total Austrian population since 1984. In this surveillance a protection rate in children of above 98% after completion of the primary vaccination schedule (3 doses) was calculated for the period 1994 to 2003. Based on a follow up surveillance performed among the total Austrian population for the years 2000 to 2006, a protection rate of 99% was calculated with no statistically significant difference between age groups in regularly vaccinated persons.
The protection rate is at least as high after the first two vaccinations, following the conventional and rapid vaccination i.e., before completion of the basic vaccination scheme by the third vaccination.

In those with a record of irregular vaccination protection rate is significantly lower.

In clinical studies with TicoVac Junior 0.25 ml, seropositivity was defined as an ELISA value >126 VIE U/ml or NT titers ≥10. Pooled seropositivity rates determined by ELISA and NT at 21 days after the second and third vaccination in the conventional schedule are presented in Table 1 and Table 2.

Table 1.
Conventional immunization schedule, pooled seropositivity rates [1] as determined by ELISA and NT

Subjects aged 1-5 years	**ELISA[2]**		**NT[2]**	
Dose	2nd	3rd	2nd	3rd
Seropositivity rate[1],% **(n/N)**	99.4 (501/504)	100.0 (493/493)	98.5 (196/199)	99.5 (193/194)

Table 2.
Conventional immunization schedule, pooled seropositivity rates [1] as determined by ELISA and NT

Subjects aged 6-15 years	**ELISA[2]**		**NT[2]**	
Dose	2nd	3rd	2nd	3rd
Seropositivity rate[1],%	97.1	99.8	95.5	99.7

Subjects aged 6-15 years	**ELISA[2]**		**NT[2]**	
Dose	2nd	3rd	2nd	3rd
(n/N)	(496/511)	(505/506)	(274/287)	(289/290)

[1] - evaluated 21 days after each dose
[2] - seropositivity cut-off: ELISA >126 VIE U/ml; NT ≥ 1:10

The highest seropositivity rates as determined by ELISA and NT were achieved upon administration of the third dose. Therefore, completion of the primary vaccination schedule of three doses is necessary to achieve protective antibody levels in almost all recipients.

5 months after the second vaccination more than 97% of children aged 1-5 years and more than 93% of children aged 6-15 years showed seropositive TBE antibody levels in both ELISA and NT.

Results from a follow-up study that investigated the persistence of TBE antibodies support the need for the first booster vaccination no later than three years after primary immunization. An analysis on seropersistence up to 58 months after the first booster showed high seropositivity rates in NT for all age subgroups: 96.6% in children aged 1-2 years, 100% in children aged 3-6 years and 98.1% in those aged 7-15 years, supporting a 5-year booster interval from the first booster onwards.

TicoVac vaccination induces statistically equivalent titers of TBE virus neutralizing antibodies against European, Siberian and Far Eastern TBE virus strains. In a published clinical study considerable cross-neutralising antibodies were also induced against Omsk Hemorrhagic Fever Virus, however titers were lower than against the TBE virus subtypes.

A study on the persistence of immune memory in individuals from the age of 6 years and older whose vaccination intervals were longer than recommended (≤12 years) showed that a single catch-up vaccination with TicoVac was able to elicit an anamnestic antibody response in 99% of children as measured by ELISA. No data are available on antibody response as measured by NT.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride , Human serum albumin, Aluminium hydroxide, hydrated, Disodium phosphate-dihydrate, Potassium dihydrogenphosphate, Sucrose, Formaldehyde, Protamine sulfate, Neomycin and gentamicin, Water for Injections.

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Keep the syringe in the outer carton in order to protect from light. Do not freeze.

6.5 Nature and contents of container

0.25 ml of suspension for injection in pre-filled syringe (type I glass) with a plunger stopper (halogenobutyl rubber). Pack sizes of 1, 10, 20 and 100 are available. The pack may include no needles or 1 separate needle per syringe. Needles are sterile and for single use only. Not all pack sizes may be marketed.

Each pre-filled syringe is packed in a blister. The opening in the blister seal is intended and allows for the equilibration of moisture during the recommended warm-up prior to the administration of the vaccine. Open the blister by removing the lid to take out the syringe. Do not press the syringe through the blister.

For subcutaneous administration, see section 6.6.

6.6 Special precautions for disposal and other handling

The vaccine should reach room temperature before administration. Shake well prior to administration to thoroughly mix the vaccine suspension. After shaking, TicoVac Junior 0.25 ml is an off-white, opalescent, homogenous suspension. The vaccine should be inspected visually for any foreign particulate matter and/or variation in physical appearance prior to administration. In the event of either being observed, discard the vaccine.

After removing the syringe cap, attach the needle immediately and remove the needle shield prior to administration. Once the needle is attached, the vaccine must be administered immediately. In the exceptional cases of subcutaneous administration, an appropriate needle should be used.

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

The administration of the vaccine should be documented by the physician, and the lot number recorded. A detachable documentation label is attached to each preloaded syringe.

7. MARKETING AUTHORISATION HOLDER

Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

8. MANUFACTURER

Pfizer Manufacturing Belgium NV, Puurs, Belgium

9. LICENSE NUMBER

162-32-35412

Revised in 10/2021 according to MOH guidelines.