SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Encepur Children (0.25 mL)
Suspension for injection in pre-filled syringe
Tick-borne encephalitis (TBE) vaccine, inactivated.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.25 mL) contains:
0.75 micrograms inactivated TBE (tick-borne encephalitis) virus, strain K23*, adsorbed on aluminium hydroxide (hydrated) (0.15 to 0.20 mg Al^{3+}).

*Host system: primary chicken embryo cells (PCEC).

Encepur Children contains trace amounts of formaldehyde, chlortetracycline, gentamycin and neomycin, and may include trace residues of egg and chicken proteins. See sections 4.3 and 4.4.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

Encepur Children is an off-white, turbid suspension for injection in a pre-filled syringe.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Active immunisation against tick-born encephalitis (TBE) virus for children from 1 year up to and including 11 years old. Encepur for adults is used for individuals over 12 years of age.
The vaccine is indicated for individuals who are temporarily or permanently in close contact with natural environments within TBE-endemic areas.

Encepur Children should be used in accordance with national recommendations.

4.2 Posology and method of administration

Posology

For children aged 1 up to and including 11 years, the same dose of 0.25 mL is given.

a) Primary immunisation:
Primary immunisation consists of 3 doses and should preferably take place during the cold seasons of the year to offer protection during the risk period (spring/summer).

Encepur Children can be administered according to the following immunisation schedule:

	Conventional schedule	Express mmunisation schedule
Dose 1	Day 0	Day 0
Dose 2	14 days to 3 months after the 1st dose*	Day 7
Dose 3	9–12 months after the 2nd vaccination dose)	Day 21

*Administration of the second dose 14 days after the first dose is referred as the fast conventional immunisation schedule in section 5.1, while administration 1 to 3 months after the first dose follows the conventional schedule.

The conventional immunisation schedule is preferable for individuals continuously at risk of infection.
The express vaccination schedule is adjusted for children who quickly need immunisation.
Seroconversion can be expected no less than 14 days after the second dose.
Once the primary immunisation schedule is complete, antibody titres are maintained for at least 12 to 18 months (according to the express primary immunisation schedule) or for at least 3 years (conventional schedule) after which the first booster dose is recommended.

See section 4.4 for additional information on vaccination of individuals with any type of impaired immune response.

b) Booster vaccination
After primary immunisation according to one of the two abovementioned schedules, one additional injection of 0.25 mL Encepur Children is sufficient to reinforce primary protection.

A booster dose must be given as follows:

Booster	Conventional schedule	express immunisation schedule
First booster dose	3 years after the last primary immunisation dose	12 to 18 months after the last primary immunisation dose
Subsequent booster doses	Every 5 years after the first booster dose	

For those over 12 years old, a TBE vaccine for adolescents and adults must be used (such as Encepur).

According to the WHO's official recommendations, Encepur Children can be given as a booster after primary immunisation with another inactivated vaccine against tick-borne encephalitis (three doses).

Method of administration
Shake the vaccine well before injection.
The vaccine must be administered intramuscularly, preferably in the upper arm (*deltoid muscle*) or anterolaterally in the thigh (depending on muscle mass).
The vaccine can be injected subcutaneously if necessary (for example in patients with haemorrhagic diathesis).
Must ***not*** be injected intravascularly.

4.3 Contraindications

Acute febrile illness.
If complications arise in conjunction with immunisation with Encepur Children, continued immunisation with Encepur Children is contraindicated until the cause of these complications is investigated.
Hypersensitivity to the active substance or any of the excipients listed in section 6.1, or to formaldehyde, chlortetracycline, gentamycin, neomycin, egg or chicken proteins.

4.4 Special warnings and precautions for use

The necessity of vaccinating individuals with severe neurological damage should be carefully considered.

As with any injection of vaccines, the usual monitoring and appropriate medical treatment must be available in case of an anaphylactic reaction after administration of the vaccine.

Children under 3 years of age may experience high fever > 39.5ºC. Treatment with antipyretics when warranted is recommended because of the risk of febrile seizures. Fever (> 38ºC) occurs primarily after the first vaccination and is less common after the second vaccination.

Encepur Children may contain trace residues of egg and chicken protein such as ovalbumin. Patients who are allergic to eggs and who have reacted with clinical symptoms, such as urticaria, swollen lips and epiglottis, laryngospasm or bronchospasm, blood pressure drop or shock after eating eggs, should be immunised only under careful clinical monitoring and with equipment for immediate emergency treatment if needed. In normal cases there is no increased risk associated with vaccination with Encepur Children for individuals classified as having “allergy to chicken protein” based solely on a questionnaire or positive prick test. Vaccination with Encepur Children normally entails no increased risk for such individuals.

Latex-sensitive individuals:

Pre-filled syringe without needle:
Despite the fact that the syringe’s tip cap does not contain natural rubber latex, safe use of Encepur Children in latex-sensitive individuals has not been established.

Pre-filled syringe with needle:
The needle shield is made from latex (natural rubber), which can cause serious allergic reactions in latex-sensitive individuals.

As with all vaccines, it is possible that a protective immune response will not be achieved in all vaccinated individuals.

It can be expected that an adequate immune response will not develop in children receiving immunosuppressive treatment and children with immune deficiency (including iatrogenic). In such cases, the antibody response should be tested using serology and an additional dose should be administered as needed.

TBE vaccination does not protect against other tick-borne diseases (such as Lyme borreliosis) even if they are transferred at the same time as the tick-borne encephalitis virus.

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation and stress-related reactions may occur in conjunction with vaccination as a psychogenic reaction to injection with needles (see section 4.8).

Encepur Children contains sodium
This medicine contains less than 1 mmol (23 mg) of sodium per dose, that is to say essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

If the vaccine is given to patients who are receiving immunosuppressive therapy, the effect of the vaccine may be reduced or uncertain.

Different injection sites must be used if more than one injectable vaccine is being administered.

Interval for other vaccinations
No interval for other vaccinations necessary.

4.6 Fertility, pregnancy and lactation

Not relevant as the vaccine is intended for children under 12 years of age.

4.7 Effects on ability to drive and use machines

Not relevant as the vaccine is intended for children under 12 years of age.

4.8 Undesirable effects

The following adverse reactions have been reported in randomised, controlled trials. Adverse reactions from clinical trials are listed by system organ class according to MedDRA. Within each organ system class, the adverse reactions are ranked by frequency, with the most common adverse reactions first. Within each frequency group, adverse reactions are presented in order of decreasing severity. In addition, the corresponding frequency category for each adverse reaction is based on the following convention (CIOMS III): very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000).

Adverse reactions reported in clinical studies

Central and peripheral nervous system disorders	
Headache in children aged 3 years and above	Very common
Drowsiness in children aged under 3 years	Very common
Gastrointestinal disorders	
Nausea	Common
Vomiting	Rare
Diarrhoea	Rare
Musculoskeletal and connective tissue disorders	
Myalgia	Common
Arthralgia	Common
General disorders and administration site conditions	
Pain at the injection site	Very common
Fever > 38ºC in children aged 1 to 2 years	Very common
Fever > 38ºC in children aged 3 to 11 years	Common
Influenza-like illness	Common
Erythema at the injection site	Common
Oedema at the injection site	Common
Malaise	Common
Lethargy	Common

Description of selected adverse reactions from clinical studies

Influenza-like illness (including hyperhidrosis, rigour, stiffness and fever) can often develop after the first vaccination but normally subsides within 72 hours.

The following adverse reactions have been identified from spontaneous post-marketing reports and are presented by system organ class. As these adverse reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency.

Adverse reactions reported in post-marketing experience

System organ class	**Undesirable effect**
Blood and lymphatic system disorders	Lymphadenopathy
Immune system disorders	Allergic reactions
Central and peripheral nervous system disorders	Paraesthesia, cerebral seizures with fever, syncope
Musculoskeletal and connective tissue disorders	Myalgia, arthralgia
General disorders and administration site conditions	Granuloma at the injection site,

Description of selected adverse reactions reported in post-marketing experience

Allergic reactions such as generalised urticaria, exudative erythema multiforme, mucosal swelling, stridor, dyspnoea, bronchospasm, hypotonia and transitory thrombocytopenia) which in some cases may be severe. Allergies may occasionally also include circulatory reactions, possibly accompanied by transitory non-specific visual disturbances.

Paraesthesia can be reported as numbness or tingling.
Myalgia and arthralgia localised in the neck region may indicate meningism. These symptoms are very rare and subside within a few days with no sequelae.

Granuloma at the injection site has occasionally been reported with formation of a seroma.

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 (see details below).

Swedish Medical Products Agency
Box 26
S-751 03 Uppsala
www.lakemedelsverket.se

In isolated cases, disorders of the central and peripheral nervous system, including an increasing level of paralysis up to respiratory paralysis (e.g. Guillain-Barré syndrome) have been reported.
Arthralgia and myalgia in the neck region can mimic symptoms of meningism. These symptoms are uncommon and subside within a few days with no sequelae.
Vaccination can, like all forms of immunostimulation, cause an exacerbation of autoimmune diseases, such as multiple sclerosis and iridocyclitis in some patients.

4.9 Overdose

Known symptoms: A significantly increased risk of adverse reactions is possible after administering a dose as low as 3 micrograms.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Encephalitis vaccine. ATC code: J07B A01

Immunogenicity in vaccinated individuals can be measured using the ELISA method, the method for measuring neutralising antibodies (NT) and the haemagglutination inhibition assay (HI). Since NT is a functional method of measurement, it is considered to be the standard method for evaluation of immunogenicity of TBE vaccine in clinical studies. In the clinical studies, a validated NT method was used in which NT > 2 indicates seropositivity and NT ≥ 10 has been chosen as the most conservative antibody limit that can be considered clinically meaningful. Immunogenicity was induced 3 weeks after fully completed primary immunisation with Encepur, analysed using the method for measuring neutralising antibodies (NT).

Primary immunisation

A total of 9 clinical studies have been conducted, ranging from phase I to phase IV, designed to evaluate the immunogenicity and safety of various primary immunisation schedules and booster schedules using Encepur Children, which included approximately 3,200 children.
The percentage of children with TBE antibody titres NT ≥ 10 and respective geometric mean titre (GMT) are shown in the table below:

Conventional immunisation schedule		Fast conventional immunisation schedule*		Express immunisation schedule	
2 weeks after dose 2					
NT ≥ 10	NT GMT	NT ≥ 10	NT GMT	NT ≥ 10	NT GMT
98%	72	91%	25	Not tested	
3 weeks after dose 3					
100%	3672	100%	3335	99%	57

*Fast conventional immunisation schedule is the conventional schedule but with the second dose given 14 days after the first dose (see section 4.2)

Duration of immune response

The length of time that antibodies persist in children is presented in the following table:

Conventional immunisation schedule		Fast conventional immunisation schedule*		Express immunisation schedule	
3 years after completed primary immunisation				3 years after the first booster vaccination	
NT ≥ 10	NT GMT	NT ≥ 10	NT GMT	NT ≥ 10	NT GMT
98%	459	96%	233	100%	475
5 years after completed primary immunisation				5 years after the first booster vaccination	
91%	244	86%	109	100%	588

*Fast conventional immunisation schedule is the conventional schedule but with the second dose given 14 days after the first dose (see section 4.2)

Published data from vaccinated individuals who received three doses of primary immunisation indicate that Encepur also induces antibodies against some East Asian isolates of TBE virus.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

The vaccine appears to be well-tolerated. No serious local or systemic harmful effects were observed after injection in the usual animal models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol
Sucrose
Sodium chloride
Water for injection.

6.2 Incompatibilities

The vaccine must not be mixed with other fluids for injection in the same syringe.

6.3 Shelf life

24 months

Use before the expiry date stated on the pack.

6.4 Special precautions for storage

Keep refrigerated (2 C to 8 C). Protect from light.

Do not freeze. Vaccine that has been frozen must not be used.

Use immediately after opening the container.

6.5 Nature and contents of container

The pre-filled syringes (type 1 glass) are fitted with a plunger stopper (bromobutyl) and a plunger (polystyrene).
The pre-filled syringes with needles (stainless steel) are fitted with a needle shield (of latex) while the pre-filled syringes without a needle have a sealing system with a luer cone with a tip cap (styrene-butadiene).

Encepur Children is provided in single-dose syringes (with or without a needle). Each syringe contains 0.25 mL. Pack size: 1 × 0.25 mL, 10 × 0.25 mL.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Shake vaccine well before use.

Parenteral medication must be visually inspected for particles and discolouration prior to administration. Vaccines with abnormal physical appearance must be discarded.

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

7. MARKETING AUTHORISATION HOLDER

Bavarian Nordic A/S
Philip Heymans Allé 3
DK-2900 Hellerup
Denmark

8. MARKETING AUTHORISATION NUMBER(S)

17432

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 November 2002
Date of latest renewal: 01 November 2007

10. DATE OF REVISION OF THE TEXT

2022-05-10