SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Encepur (0.5 mL)
Suspension for injection in pre-filled syringe
Tick-borne encephalitis (TBE) vaccine, inactivated.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:
1.5 micrograms inactivated TBE (tick-borne encephalitis) virus, strain K23*, adsorbed on aluminium hydroxide (hydrated) (0.3 to 0.4 mg Al^{3+}).

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

Encepur 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 the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Active immunisation against tick-borne encephalitis (TBE) virus for individuals from 12 years and up.
The vaccine is indicated for individuals who are temporarily or permanently in close contact with natural environments within TBE-endemic areas.

Encepur should be used in accordance with national recommendations

4.2 Posology and method of administration

Posology

0.5 mL for adolescents and adults from ages 12 years and up.

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 can be administered according to the following immunisation schedule:

	Conventional schedule	Express immunisation 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 to as the fast conventional immunisation schedule in section 5.1, while administration 1 to 3 months after the first dose follows the conventional schedule.

Seroconversion can be expected no less than 14 days after the second dose of vaccine. Once the primary immunisation schedule is complete, antibody titres are maintained for at least 12 to 18 months (after the express 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 vaccination schedules, a booster dose should be given as follows:

Express immunisation schedule		
	First booster dose	Subsequent booster doses
12 to 49 years old	12 to 18 months after the last primary immunisation dose	Every 5 years
> 49 years old	12 to 18 months after the last primary immunisation dose	Every 3 years
Conventional schedule		
	First booster dose	Subsequent booster doses
12 to 49 years old	3 years after the last primary immunisation dose	Every 5 years
> 49 years old	3 years after the last primary immunisation dose	Every 3 years

According to the WHO’s official recommendations, Encepur can be given as a booster after primary immunisation with another inactivated vaccine against tick-borne encephalitis (3 doses).

Method of administration
Shake the vaccine well before injection.
The vaccine should be administered intramuscularly, preferably in the upper arm *(deltoid muscle).* 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.
Should complications occur after immunisation with Encepur, additional vaccinations with Encepur should be considered contraindicated until the cause of the complication has been 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.

Encepur 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 for individuals classified as having “allergy to chicken protein” based solely on a questionnaire or positive prick test. Vaccination with Encepur 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 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 patients receiving immunosuppressive treatment and patients with immune deficiency (including iatrogenic and age-related). 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). It is important for procedures to be in place to avoid injury upon fainting.

Encepur contains sodium
This medicine contains less than 1 mmol sodium (23 mg) 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.

<u>Interval for other vaccinations</u>
No interval for other vaccinations necessary.

4.6 Fertility, pregnancy and lactation

There is no clinical experience in pregnant and breast-feeding women. No data are available from animal studies.
There are no data available on excretion into human milk.
Encepur should be given to pregnant and nursing women only after careful consideration of the risks and benefits to the mother and the child.

4.7 Effects on ability to drive and use machines

Encepur has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse reactions were reported in 3,223 trial participants recruited to 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	Very common
Gastrointestinal disorders	
Nausea	Common
Vomiting	Uncommon
Musculoskeletal and connective tissue disorders	
Myalgia	Very common
Arthralgia	Common
General disorders and administration site conditions	
Pain at the injection site	Very common
Malaise	Very common
Fever > 38ºC	Common
Erythema, oedema at the injection site	Common
Influenza-like symptoms	Common

Description of selected adverse reactions from clinical studies
Influenza-like symptoms (including fever, hyperhidrosis, rigour, stiffness) occur, particularly after the first vaccination. These symptoms usually subside 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, dizziness, presyncope, syncope
Gastrointestinal disorders	Diarrhoea
Musculoskeletal and connective tissue disorders	Myalgia, arthralgia
General disorders and administration site conditions	Granuloma at the injection site, fatigue, asthenia

Description of selected adverse reactions reported in post-marketing experience
Allergic reactions such as generalised urticaria, angioedema, stridor, dyspnoea, bronchospasm, hypotonia) and other circulatory reactions, possibly accompanied by transitory, non-specific visual disturbances and transitory thrombocytopenia, which can sometimes be severe.

Paraesthesia can be reported as numbness or tingling.
Granuloma at the injection site has occasionally been reported with formation of a seroma.
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.

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

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

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.

Primary immunisation

A total of 12 clinical studies, ranging from phase I to phase IV, have been designed to evaluate the immunogenicity and safety of various primary immunisation schedules and booster schedules with Encepur and included more than 2,600 adolescents and adults.
The percentage of trial subjects with TBE antibody titres NT≥10 and respective geometric mean titre (GMT) are shown in the table below:

Fast conventional immunisation schedule	Conventional immunisation schedule	Express immunisation schedule
4 weeks after dose 2	2 weeks after dose 2	

NT ≥ 10	NT GMT	NT ≥ 10	NT GMT	NT ≥ 10	NT GMT
79%	23	95%	66	79%	23
3 weeks after dose 3					
100%	1 107	100%	1 155	97%	51

*Fast conventional schedule is the conventional schedule but with the second dose given 14 days after the first dose.

Seroconversion can be expected within approximately 14 days after vaccination dose 2 when the express immunisation schedule is used.

Booster vaccination

The percentage of adolescents and adults with TBE antibody titres NT ≥ 10 after booster is shown in the table below:

10 years after booster dose	NT ≥ 10: > 97% regardless of which primary immunisation schedule has been used. NT GMT: 260 to 301

NT and GMT values were each independent of the primary immunisation schedule.

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

2 years

Use before the expiry date stated on the pack.

6.4 Special precautions for storage

Store at 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).

Pre-filled syringe (with or without needle) containing 0.5 mL suspension.

- Pack with 1 pre-filled syringe (with/without needles) each containing 0.5 mL suspension
- Pack with 10 pre-filled syringes (with/without needles) each containing 0.5 mL suspension
- Pack with 20 pre-filled syringes (with/without needles) each containing 0.5 mL suspension (2 × 10 packs)

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)

13472

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 October 1998
Date of latest renewal: 05 December 2006

10. DATE OF REVISION OF THE TEXT

2022-05-10