# PATIENT INFORMATION LEAFLET

**NAVILIZE 100 mg/ml can seriously harm an unborn child when received during pregnancy. It can cause serious birth defects to body organs and/or body structures as well as harm the developing brain of the fetus and can also affect the way in which the child develops as it grows.**
**Children whose mothers received NAVILIZE 100 mg/ml during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, be intellectually less able than other children, and have difficulties with language and memory.**
**Children whose mothers received NAVILIZE 100 mg/ml during pregnancy have an increased risk of developing autistic spectrum disorders, childhood autism and attention-deficit hyperactivity disorder (ADHD).**
**NAVILIZE 100 mg/ml treatment must be started and supervised by a medical practitioner experienced in the treatment of epilepsy. You must not receive NAVILIZE 100 mg/ml if the risk minimisation measures have not been explained to you and if you cannot commit to follow the pregnancy risk minimisation measures.**

## SCHEDULING STATUS

**S3**

**NAVILIZE 100 mg/ml solution for injection or infusion**

**Sodium valproate**

**Sugar free**

**Read all of this leaflet carefully before you are given NAVILIZE 100 mg/ml.**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or

other health care provider.

- NAVILIZE 100 mg/ml has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

**What is in this leaflet**



## 1. What NAVILIZE 100 mg/ml is and what it is used for

NAVILIZE 100 mg/ml contains sodium valproate which is a medicine used to for the treatment of epilepsy in adults and children. Epilepsy is a condition where you have repeated seizures (fits). There are many different types of seizures, ranging from mild to severe. NAVILIZE 100 mg/ml belongs to a group of medicines called anticonvulsants. These medicines are thought to work by controlling brain chemicals which send signals to nerves so that seizures do not happen. NAVILIZE 100 mg/ml may be used alone or in combination with other medicines to treat your condition. NAVILIZE 100 mg/ml may be used short term in place of oral sodium valproate tablets or liquid when the medicine cannot be given by mouth.

## 2. What you need to know before you receive NAVILIZE 100 mg/ml

**NAVILIZE 100 mg/ml should not be administered to you:**

- If you are hypersensitive (allergic) to sodium valproate or any of the other ingredients of NAVILIZE 100 mg/ml (listed in section 6).

- If you have or have had liver disease (hepatic dysfunction) or a family history of severe hepatitis, especially when caused by medicines. Medicines used in the treatment of epilepsy, including NAVILIZE 100 mg/ml may have adverse effects on the liver and kidneys.
- If you have a urea cycle disorder or a family history of urea cycle disorders.
- If you are pregnant or breastfeeding (see Warnings and Special precautions and Pregnancy, Breastfeeding and Fertility sections below).
- If you are a woman of childbearing potential (there is a chance that you might become pregnant), unless the other treatments didn't work the way it is supposed to work or if you cannot take those medicines.
- If you have porphyria which is a rare blood disease of blood pigments.
- If you have known or suspected of having a genetic problem causing a mitochondrial disorder (POLG e.g. Alpers-Huttenlocher Syndrome).

**Warnings and precautions**

A small number of people being treated with anti-epileptics such as sodium valproate (as in NAVILIZE 100 mg/ml) have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

Convulsions may become worse or happen more frequently whilst receiving NAVILIZE 100 mg/ml. If this happens contact your doctor immediately.

**Tell your doctor or health care provider before being given the injection:**

- If you are a female patient of childbearing age, make sure that you talk to your doctor about the risks associated with receiving NAVILIZE 100 mg/ml during pregnancy. Tel your doctor if you are pregnant or intent to become pregnant.
- If you are breastfeeding or planning to breastfeed. Your doctor will discuss the risks and benefits of taking it if you are breastfeeding or planning to breastfeed.

- If you drink alcohol, (more than 2 drinks per day), you may be putting yourself at risk of a seizure, or fit.
- If you have liver problems. Your doctor may need to monitor your liver function more carefully.
- If you have kidney problems. Your doctor may give you a lower dos if you have diabetes. This medicine may affect the results of urine tests.
- If you have a brain disease or a metabolic condition affecting your brain.
- If you have a 'urea cycle disorder' where too much ammonia builds up in the body.
- If you have an illness called systemic lupus erythematosus (a disease of the immune system which affects the skin, joints and kidneys).
- If you have an ornithine transcarbamylase (OTC) deficiency.
- If you have a known, suspected or family history of mitochondrial disease (POLG e.g. Alpers-Huttenlocher Syndrome).
- If you have an underlying carnitine palmitoyltransferase (CPT) type II deficiency.
- If you plan to have surgery.

*Weight gain*

Receiving NAVILIZE 100 mg/ml may make you put on weight. Talk to your doctor about how this will affect you.

*Blood tests*

Your doctor may wish to do blood tests before you start receiving NAVILIZE 100 mg/ml and during your treatment.

**Other medicines and NAVILIZE 100 mg/ml**

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Some medicines and NAVILIZE 100 mg/ml may interfere with each other. These include:

- Aspirin and other salicylates (used for pain and inflammation).
- Medicines used to prevent clots (anticoagulants) e.g. warfarin.
- Other medicines used to treat epilepsy e.g. phenobarbitone, methylphenobarbitone, primidone, phenytoin, carbamazepine, clonazepam, felbamate, lamotrigine, topiramate, diazepam, lorazepam, oxcarbamazepine, and ethosuximide.
- Medicines used to treat depression e.g. monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants.
- Benzodiazepines (medicines used as sedatives or to treat anxiety).
- Oral contraceptives. NAVILIZE 100 mg/ml should have little effect on the oral contraceptive pill, however, you should let your doctor know that you are taking it.
- Zidovudine or any other anti-viral medications (used to treat HIV infection).
- Antipsychotic medicines including clozapine (a medicine used to treat schizophrenia).
- Quetiapine or olanzapine (a medicine used to treat bipolar disorder and schizophrenia).
- Mefloquine (a medicine used to treat malaria).
- Propofol (a medicine used before and during general anaesthesia).
- Nimodipine (a medicine used to help blood flow to the brain).
- Cimetidine (used to treat stomach ulcers).
- Carbapenem agents (antibiotics used to treat bacterial infections) such as imipenem, meropenem, rifampicin and erythromycin.
- Cholestyramine (used to lower cholesterol).
- Acetazolamide (used to treat diabetes).

These medicines and others may be affected by NAVILIZE 100 mg/ml or may affect how well it works. You may need different amounts of your medicine, or you may need to take different medicines. Your doctor or pharmacist will advise you.

**NAVILIZE 100 mg/ml with alcohol**

The effects of alcohol could be made worse while you are receiving NAVILIZE 100 mg/ml. Combining it and alcohol can make you more sleepy, dizzy or lightheaded. Your doctor may suggest you avoid alcohol while you are treated with NAVILIZE 100 mg/ml.

**Pregnancy, breastfeeding and fertility**

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

***Pregnancy***

If you are a female patient of childbearing age, make sure that you talk to your doctor about the risks associated with receiving NAVILIZE 100 mg/ml during pregnancy. Tel your doctor if you are pregnant or intent to become pregnant. NAVILIZE 100 mg/ml may affect your developing baby if taken in the first trimester of pregnancy, as it is suspected of causing an increased risk of malformations in the exposed foetus. Also, children born to mothers who receive NAVILIZE 100 mg/ml throughout their pregnancy may be at risk of impaired cognitive development or withdrawal syndrome. Your doctor will discuss the risks and benefits of receiving it if you are pregnant.

***Breastfeeding***

If you are breastfeeding or planning to breastfeed, medicines used in the treatment of epilepsy, including NAVILIZE 100 mg/ml, pass into breast milk. Your doctor will

discuss the risks and benefits of taking it if you are breastfeeding or planning to breastfeed.

***Fertility***

NAVILIZE 100 mg/ml can cause infertility in both men and women that may not always be reversible.

*Female patients*

With the use of NAVILIZE 100 mg/ml, you may experience absence of menstruation or a hormonal condition (polycystic ovaries) that affects your ovaries and can cause you ovaries to produce too many male sex hormones which will influence your fertility.

*Male patients*

Your doctor will have explained to you the known risk of male infertility and the potential risk in children born to fathers treated with NAVILIZE 100 mg/ml.

As a precautionary measure, your doctor will discuss with you:

- The potential risk in children born to fathers treated with valproate
- The need to use effective contraception (birth control) for you and your female partner during treatment and for 3 months after stopping treatment
- The need to consult your doctor when you are planning to conceive a child and before stopping contraception (birth control)
- The possibility of other treatments that can be used to treat your disease, depending on your individual situation

Do not donate sperm when receiving NAVILIZE 100 mg/ml or for 3 months after stopping the treatment.

Talk to your doctor if you are thinking about having a baby.

If your female partner becomes pregnant while you received NAVILIZE 100 mg/ml in the 3 months period before conception and you have questions, contact your doctor.

**Driving and using machines**

Be careful when driving or operating machinery until you know how NAVILIZE 100 mg/ml affects you. It may cause drowsiness in some people. Make sure you know how you react to NAVILIZE 100 mg/ml before you drive a car, operate machinery or do anything else that could be dangerous if you are drowsy or light-headed.

## 3. How to receive NAVILIZE 100 mg/ml

Do not share medicines prescribed for you with any other person.

You will not be expected to give yourself NAVILIZE 100 mg/ml. It will be given to you by a person who is qualified to do so.

Each ampoule of NAVILIZE 100 mg/ml is for single dose injection only. NAVILIZE 100 mg/ml will be given to you as an infusion or injection into the veins. Your doctor will stop giving you NAVILIZE 100 mg/ml and change you to sodium valproate tablets, liquid or syrup as soon as possible.

Your doctor will decide what dose of NAVILIZE 100 mg/ml you need, and this will be given under close supervision, usually in a hospital setting. Your doctor will decide how much to give you depending on your illness. The amount of NAVILIZE 100 mg/ml given to you or your child will depend on you or your child’s age or body weight.

If you are currently taking an oral formulation of NAVILIZE (tablets, liquid or syrup) and are now changing over to NAVILIZE, the total daily dose of NAVILIZE should remain the same.

***Adults***

The starting dose is usually 600 mg per day, increasing by 200 mg per day at three-day intervals until control is achieved. If adequate control has not been achieved in two weeks, the dose may be further increased in stages to a maximum of 2 500 mg each day.

***Children over 20 kg***

The starting dose is 400 mg per day irrespective of weight in divided doses until control is achieved. This is usually 20 to 30 mg for each kg of body weight every day. If epilepsy is not controlled the dose may be increased up to 35 mg for each kg of body weight every day, as long as blood tests are done to check the amount of NAVILIZE 100 mg/ml in the blood.

***Children under 20 kg***

The usual dose is 20 mg for each kg of body weight per day.

Your doctor will tell you how long your treatment with NAVILIZE 100 mg/ml will last. If you have the impression that the effect of NAVILIZE 100 mg/ml is too strong or too weak, tell your doctor or pharmacist.

**If you receive more NAVILIZE 100 mg/ml than you should**

Since a health care provider will administer NAVILIZE 100 mg/ml, he/ she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

Signs of overdosage or receiving too much NAVILIZE 100 mg/ml include:

- Coma, poor muscle tone resulting in limpness of the body.
- Inability to breathe properly.
- Having little or no reflexes when tested using a reflex hammer.
- Constriction of the pupils – pupils become smaller.
- Seizures.
- Very high pressure within the skull.
- Death may occur in case of a large overdose.

**If you forget to receive NAVILIZE 100 mg/ml**

Since a health care provider will administer NAVILIZE 100 mg/ml, it is unlikely that the dose will be missed.

**If you stop receiving NAVILIZE 100 mg/ml**

It is important for you to keep having NAVILIZE 100 mg/ml until your doctor decides to stop them. If you stop, your fits may come back.

## 4. Possible side effects

NAVILIZE 100 mg/ml can have side effects.

Not all side effects reported for NAVILIZE 100 mg/ml are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving NAVILIZE 100 mg/ml, please consult your health care provider for advice.

If any of the following happens, stop receiving NAVILIZE 100 mg/ml and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, tongue and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to NAVILIZE 100 mg/ml. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest

hospital if you notice any of the following:

- more frequent or more severe seizures (fits),
- blood clotting problems,
- spontaneous bruising or bleeding,
- signs of liver problems such as vomiting, loss of appetite, generally feeling unwell, tiredness, yellowing of the skin and/or eyes, dark urine or blood in urine, pain in the abdomen,
- bizarre behaviour, suicidal thoughts, suicide attempts,
- severe upper stomach pain, often with nausea, vomiting and/or loss of appetite especially when prolonged.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following side effects:

*Frequent*

- nausea or vomiting, diarrhoea,
- abdominal cramps or pain,
- bleeding, tender or enlarged gums,
- changes in appetite,
- increases in your weight,
- irregular menstrual periods,
- headache,
- hearing loss,
- unusual movements, including tremor and shaking,
- rapid uncontrollable movements of the eye,
- unsteadiness when walking, dizziness or light-headedness,
- hair loss,
- feeling tired or drowsy,

- memory impairment, confusion, hallucinations,
- disturbance in attention,
- changes in behaviour including aggression and agitation,
- nail and nailbed disorders.

*Less frequent*

- depression,
- skin problems such as rashes,
- hair disorders (changes in texture, colour or growth),
- increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest, acne or thinning hair,
- skin rash caused by narrow or blocked blood vessels (vasculitis),
- swelling of the feet and legs (oedema),
- obesity, weight gain – as your appetite may be increased,
- kidney disease, kidney problems, blood in the urine, bedwetting or increased need to pass urine, urinary incontinence (unintentional passing of urine),
- restlessness/hyperactivity and learning disorder,
- tingling or numbness of the hands or feet,
- lowering of normal body temperature,
- muscle pain and weakness (rhabdomyolysis),
- bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures.

*Frequency unknown:*

- changes in women's periods and increased hair growth in women,
- breast enlargement in men,
- skin rash or skin lesions, especially on your palms or soles of your feet, with a

pink/red ring and a pale centre which may be itchy, scaly or filled with fluid (erythema multiforme),

- blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals; also flu-like symptoms and fever (Stevens-Johnson syndrome),
- severe blistering rash where layers of the skin may peel off to leave large areas of raw exposed skin over the body; also a feeling of being generally unwell, fever, chills and aching muscles (toxic epidermal necrolysis).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

**Reporting of side effects**

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

By reporting side effects, you can help provide more information on the safety of NAVILIZE 100 mg/ml.

## 5. How to store NAVILIZE 100 mg/ml

Store all medicines out of reach of children.

- Store at or below 30 °C
- After opening, use as soon as practicable. If storage is necessary, hold at 2 to 8 ºC for not more than 24 hours.
- Do not use after the expiry date stated on the label / carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

## 6. Contents of the pack and other information

### What NAVILIZE 100 mg/ml contains

- The active substance is sodium valproate. Each ml contains 100 mg sodium valproate.
- The other ingredients are disodium phosphate dodecahydrate, potassium dihydrogen phosphate and water for injections.

### What NAVILIZE looks like and contents of the pack

NAVILIZE 100 mg/ml is a clear liquid and particles free in a colourless glass ampoule.

NACACON 100 mg/ml solution for injection or infusion is packed in type I transparent glass ampoules of 5 ml and 10 ml.

- 3 ml of solution packed in 5 ml capacity glass ampoule.
- 4 ml of solution packed in 5 ml capacity glass ampoule.
- 10 ml of solution packed in 10 ml capacity glass ampoule.

Pack sizes: 1, 4 or 5 ampoules placed in a white plastic tray per outer cardboard box. Not all pack sizes may be marketed.

### Holder of Certificate of Registration

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**Access to the corresponding Professional Information**

Website Address: www.trinitypharma.co.za