Package leaflet: Information for the patient
Sodium Valproate 100mg/ml Solution for Injection or Infusion
sodium valproate

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

WARNING
Sodium Valproate can seriously harm an unborn baby when taken during pregnancy.
If you are a female able to have a baby, you must use effective method of birth control (contraception) at all times without interruptions during your entire treatment with Sodium Valproate Injection. Your doctor will discuss this with you but you must also follow the advice in section 2 of this leaflet.
Schedule an urgent appointment with your doctor or nurse if you want to become pregnant or if you think you are pregnant.
Do not stop taking Sodium Valproate Injection unless your specialist tells you to as your condition may become worse.
If you are a parent or caregiver of a female child treated with Sodium Valproate Injection, you must also read section 2 of this leaflet carefully and contact your child's doctor or nurse once they experience their first period.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Sodium Valproate Injection is and what it is used for

What Sodium Valproate Injection is
The name of your medicine is Sodium Valproate 100mg/ml Solution for Injection or Infusion
(called Sodium Valproate Injection in this leaflet).

What Sodium Valproate Injection contains
Sodium Valproate Injection contains a medicine called sodium valproate. This belongs to a group of medicines called anti-convulsants or anti-epileptic agents. It works by helping to calm the brain down.

What Sodium Valproate Injection is used for
Sodium Valproate Injection is used to treat epilepsy (fits) in adults and children. The injection is given when it is not possible to have your medicine by mouth.

2. What you need to know before you are given Sodium Valproate Injection

Do not have Sodium Valproate Injection and tell your doctor or nurse if:
- You are allergic (hypersensitive) to sodium valproate or any of the other ingredients of Sodium Valproate Injection (listed in section 6)
  Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- You have a known metabolic disorder, i.e a urea cycle disorder
- You have liver problems or you or your family have a history of liver problems, especially if caused by taking a medicine
- You have a rare illness called porphyria which affects your metabolism
- You have a genetic problem caused by a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
- You have a deficiency in carnitine (a very rare metabolic disease) that is untreated
- You are pregnant, unless nothing else works for you (see 'Pregnancy, breast-feeding and fertility – Important advice for women' below).

If you are a woman able to have a baby, you must not take Sodium Valproate Injection unless you use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection. Do not stop taking Sodium Valproate Injection or your contraception, until you have discussed this with your specialist. Your specialist will advise you further (see below under "Pregnancy, breast-feeding and fertility – Important advice for women").

Do not have this medicine if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before having Sodium Valproate Injection.

CONTACT A DOCTOR IMMEDIATELY:
- Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme and angioedema have been reported in association with valproate treatment. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Warnings and precautions
- The risk of liver damage is increased if Sodium Valproate Injection is taken by children under 3 years of age, in people taking other anti-epileptic medicine at the same time or having other neurological or metabolic disease and severe forms of epilepsy
- A small number of people being treated with anti-epileptics such as sodium valproate have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor
- As with other anti-epileptic drugs, convulsions may become worse or happen more frequently whilst taking this medicine. If this happens contact your doctor immediately
- If you or your child taking Sodium Valproate injection develops problems with balance and co-ordination, feeling lethargic or less alert, vomiting, tell your doctor immediately. This may be due to increased amount of ammonia in the blood.

Talk to your doctor, nurse or pharmacist before taking Sodium Valproate Injection if:
- You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking valproate
- You have a brain disease or a metabolic condition affecting your brain
- You have problems with your pancreas
- You have diabetes or are being tested for diabetes. This medicine may affect the results of urine tests
- You know or your doctor suspects that there is a genetic problem caused by a mitochondrial disorder in your family, because of a risk of damage to your liver
- You are suspected to suffer from any metabolic disorders, particularly hereditary enzyme deficiency disorders such as a "urea cycle disorder" because of a risk of increased ammonia level in the blood
- You have a rare disorder named "carnitine palmitoyltransferase type II deficiency" because you are at increased risk of muscle disorders
- You have impaired dietary intake in carnitine, found in meat and dairy products, especially in children less than 10 years old
- You have a deficiency in carnitine and are taking carnitine
- You have kidney problems. Your doctor may monitor your valproate level or adjust your dose
- You have an illness called 'systemic lupus erythematosus (SLE)' – a rare disease of the immune system which affects skin, bones, joints and internal organs.

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before having Sodium Valproate Injection.

Weight gain
Having Sodium Valproate Injection may make you put on weight. Talk to your doctor or nurse about how this will affect you.

Blood tests
Your doctor may request blood tests and liver function tests before and during your treatment with this medicine. Sodium Valproate Injection can change the levels of liver enzymes shown up in blood tests. This can mean that your or your child's liver is not working properly.

Other medicines and Sodium Valproate Injection
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Sodium Valproate Injection can affect the way some other medicines work. Also some medicines can affect the way Sodium Valproate Injection works.

In particular, check with your doctor if you are taking any of the following:
- Some medicines used for pain and inflammation (salicylates) such as aspirin
- Clozapine (to treat mental health conditions)Some other medicines used to treat fits (epilepsy) – see Section 3: 'Patients taking other medicines for fits'. This includes medicines such as phenobarbital, primidone, phenytoin, carbamazepine, rufinamide, topiramate, acetazolamide, lamotrigine and felbamate
- Cannabidiol (used to treat epilepsy and other conditions)
- Medicines used to calm emotional and mental health disorders (including schizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine
- Monoamine oxidase inhibitors (MAOIs) such as moclobemide (used to treat depression and anxiety), selegiline (used to treat Parkinson's disease), linezolid (used to treat infections)
- Anticoagulants – such as warfarin - used to thin the blood and prevent clots. Your doctor may change your dose of the blood thinning medicine and monitor your treatment closely
- Zidovudine and protease inhibitors such as lopinavir and ritonavir - used to treat HIV infection and AIDs
- Carbapenem agents (antibiotics used to treat bacterial infections) such as panipenem, imipenem, meropenem, rifampicin and erythromycin. The combination of Sodium Valproate Injection and carbapenems should be avoided because it may decrease the effect of your medicine
- Some anti-infectives that contain pivalate (e.g. pivampicillin, adefovir dipivoxil)
- Some medicines used to treat or prevent malaria such as mefloquine and chloroquine
- Temozolomide - used to treat cancer
- Cimetidine - used to treat stomach ulcers
- Cholestyramine - used to lower blood fat (cholesterol) levels
- Nimodipine – used to treat bleeding in the brain (subarachnoid haemorrhage)
- Propofol – used for anaesthesia
- Oestrogen-containing products (including some birth control pills)
- Metamizole – used to treat pain and fever
- Methotrexate- used to treat cancer and inflammatory diseases.

Sodium Valproate Injection with food and drink
Alcohol intake is not recommended during treatment.

Pregnancy, breast-feeding and fertility

Important advice for women
- You must not use Sodium Valproate Injection if you are pregnant, unless your specialist has determined that no alternative treatment works for you
- If you are a woman able to have a baby, you must not take Sodium Valproate Injection unless you use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection
- Do not stop taking Sodium Valproate Injection or your birth control (contraception), until you have discussed this with your specialist. Your specialist will advise you further.

The risks of valproate when taken during pregnancy
- Talk to your doctor immediately if you are planning to have a baby or are pregnant
- Valproate carries a risk if taken during pregnancy. The higher the dose, the higher the risks but all doses carry a risk, including when valproate is used in combination with other medicines to treat epilepsy
- It can cause serious birth defects and can affect the physical and mental development of the child as it grows after birth. If you take valproate during pregnancy you have a higher risk than other women of having a child with birth defects that require medical treatment. Because valproate has been used for many years, we know that in women who take valproate around 11 babies in every 100 will have birth defects. This compares to 2-3 babies in every 100 born to women from the general population
  - The most frequently reported birth defects include *spina bifida* (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects and multiple associated malformations affecting several organs and parts of the body. Birth defects may result in disabilities which may be severe
  - Hearing problems or deafness have been reported in children exposed to valproate during pregnancy
  - Eye malformations have been reported in children exposed to valproate during pregnancy in association with other congenital malformations. These eye malformations may affect vision.
- It is estimated that up to 30-40% of children whose mothers took valproate during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, intellectually less able than other children, and have difficulty with language and memory
  - Autism and related disorders are more often diagnosed in children exposed to valproate during pregnancy and there is some evidence that children exposed to valproate during pregnancy are at increased risk of developing Attention Deficit Hyperactivity Disorder (ADHD).
- Before prescribing this medicine to you, your specialist will have explained what might happen to your baby if you become pregnant whilst taking valproate. If you decide later that you want to have a baby you must not stop taking your medicine or your method of birth control (contraception) until you have discussed this with your specialist
- If you are a parent or a caregiver of a female child treated with valproate, you must contact their doctor once your child using valproate experiences their first period (menarche)
- Some birth control pills (oestrogen-containing birth control pills) may lower valproate levels in your blood. Make sure you talk to your doctor about the method of birth control (contraception) that is the most appropriate for you
- Ask your doctor or nurse about taking folic acid when planning to have a baby. Folic acid can lower the general risk of *spina bifida* and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Please choose the situations which apply to you and read the descriptions below:
- o I AM STARTING TREATMENT WITH SODIUM VALPROATE INJECTION
- o I AM TAKING SODIUM VALPROATE INJECTION AND NOT PLANNING TO HAVE A BABY
- o I AM TAKING SODIUM VALPROATE INJECTION AND PLANNING TO HAVE A BABY
- o I AM PREGNANT AND I AM TAKING SODIUM VALPROATE INJECTION.

I AM STARTING TREATMENT WITH SODIUM VALPROATE INJECTION

If this is the first time you have been prescribed valproate your specialist will have explained the risks to an unborn child if you become pregnant. Once you are able to have a baby, you must use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection. Talk to your doctor or family planning clinic if you need advice on birth control (contraception).

Key messages:
- Pregnancy must be excluded before start of treatment with Sodium Valproate Injection with the result of a pregnancy test, confirmed by your specialist
- You must use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection
- You must discuss appropriate and effective methods of birth control (contraception) with your doctor. Your doctor will give you information on preventing pregnancy, and may refer you to a specialist for advice on birth control (contraception)
- You must get regular (at least annual) appointments with a specialist experienced in the management of epilepsy. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice related to the use of valproate during pregnancy
- Tell your doctor if you want to have a baby
- Tell your doctor **immediately** if you are pregnant or think you might be pregnant.

I AM TAKING SODIUM VALPROATE INJECTION AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with valproate but you are not planning to have a baby, you must use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection. Talk to your doctor or family planning clinic if you need advice on birth control (contraception).

Key messages:
- You must use an effective method of birth control (contraception) at all times during your entire treatment with Sodium Valproate Injection
- You must discuss appropriate and effective methods of birth control (contraception) with your doctor. Your doctor will give you information on preventing pregnancy, and may refer you to a specialist for advice on birth control (contraception)
- You must get regular (at least annual) appointments with a specialist experienced in the management of epilepsy. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice related to the use of valproate during pregnancy
- Tell your doctor if you want to have a baby
- Tell your doctor **immediately** if you are pregnant or think you might be pregnant.

I AM TAKING SODIUM VALPROATE INJECTION AND PLANNING TO HAVE A BABY

If you are planning to have a baby, first schedule an appointment with your doctor.
Do not stop taking Sodium Valproate Injection or your birth control (contraception), until you have discussed this with your specialist. Your specialist will advise you further.

Babies born to mothers who have been on valproate are at serious risk of birth defects and problems with development (behaviour and learning disorders) which can be seriously debilitating. Your doctor will refer you to a specialist experienced in the management of epilepsy, so that alternative treatment options are evaluated early on. Your specialist can put several actions in place so that your pregnancy goes as smoothly as possible and any risks to you and your unborn child are reduced as much as possible.

Your specialist may decide to change the dose of valproate, switch you to another medicine, or stop treatment with Sodium Valproate Injection a long time before you become pregnant – this is to make sure your illness is stable.

Ask your doctor or nurse about taking folic acid when planning to have a baby. Folic acid can lower the general risk of *spina bifida* and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Key messages:
- Do not stop taking Sodium Valproate Injection unless your specialist tells you to
- Do not stop using your birth control (contraception) before you have talked to your specialist and worked together on a plan to ensure your epilepsy is controlled and the risks to you and your baby are reduced
- First schedule an appointment with your specialist. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice related to the use of valproate during pregnancy
- Your specialist will try to switch you to another medicine, or stop treatment with Sodium Valproate Injection a long time before you become pregnant
- Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant.

I AM PREGNANT AND I AM USING SODIUM VALPROATE INJECTION

Do not stop taking Sodium Valproate Injection, unless your specialist tells you to as your condition may become worse.

Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant. Your doctor will advise you further.

Babies born to mothers who have been on valproate are at serious risk of birth defects and problems with development (behaviour and learning disorders) which can be seriously debilitating and/or permanent.

You will be referred to a specialist experienced in the management of epilepsy, so that alternative treatment options can be evaluated.

THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY

Sodium Valproate 100mg/ml Solution for Injection or Infusion
Please refer to the Summary of Product Characteristics (SmPC) for further details on this product.

Qualitative and Quantitative Composition
Each ml of solution contains 100mg sodium valproate. Each 4ml ampoule contains 400mg sodium valproate. Each 10ml ampoule contains 1000mg sodium valproate.
For a full list of excipients; see Pharmaceutical Particulars section below.

Pharmaceutical Form
Solution for injection or infusion. A clear, colourless solution.

Posology and Method of Administration
Posology
Daily dosage requirements vary according to age and body weight.

Adults
Patients already satisfactorily treated with oral sodium valproate may be continued at their current dosage using continuous or repeated infusion. Other patients may be given a slow intravenous injection over 3-5 minutes, usually 400-800mg depending on body weight (up to 10mg/kg) followed by continuous or repeated infusion up to a maximum of 2500mg/day.

Sodium Valproate Injection should be replaced by oral valproate therapy as soon as practicable.

Special populations

Paediatric population
Daily requirement for children is usually in the range 20 – 30mg/kg/day and method of administration is as above. Where adequate control is not achieved within this range, the dose may be increased up to 40mg/kg/day but only in patients in whom plasma valproic acid levels can be monitored. In children requiring doses higher than 40mg/kg/day, clinical chemistry and haematological parameters should be monitored.

Elderly
Although the pharmacokinetics of sodium valproate are modified in the elderly, they have limited clinical significance and dosage should be determined by seizure control. The volume of distribution is increased in the elderly and because of decreased binding to serum albumin, the proportion of free drug is increased. This will affect the clinical interpretation of plasma valproic acid levels.

Renal impairment
It may be necessary in patients with renal insufficiency to decrease the dosage, or to increase the dosage in patients on haemodialysis. Sodium valproate is dialysable (see SmPC section 4.9). Dosing should be modified according to clinical monitoring of the patient (see SmPC section 4.4), since monitoring of plasma concentrations may be misleading (see SmPC section 5.2).

Hepatic impairment
Salicylates should not be used concomitantly with sodium valproate since they employ the same metabolic pathway (see SmPC sections 4.4 and 4.8).

Liver dysfunction, including hepatic failure resulting in fatalities, has occurred in patients whose treatment included valproic acid (see SmPC section 4.3 and 4.4).

Salicylates should not be used in children under 16 years of age (see aspirin/salicylate product information on Reye's syndrome). In addition in conjunction with sodium valproate, concomitant use in children under 3 years of age can increase the risk of liver toxicity (see SmPC section 4.4).

Female children and women of childbearing potential:
Valproate must be initiated and supervised by a specialist experienced in the management of epilepsy. Valproate should not be used in female children and women of childbearing potential unless other treatments are ineffective or not tolerated (see SmPC sections 4.3, 4.4 and 4.6).
Valproate is prescribed and dispensed according to the Valproate Pregnancy Prevention Programme (see SmPC sections 4.3 and 4.4). The benefits and risks should be carefully reconsidered at regular treatment reviews (see SmPC section 4.4).
Valproate should preferably be prescribed as monotherapy and at the lowest effective dose, if possible as a prolonged release formulation. The daily dose should be divided into at least two single doses (see SmPC section 4.6).

Combined therapy (see SmPC section 4.5)
When starting Sodium Valproate Injection in patients already on other anticonvulsants, these should be tapered slowly; initiation of Sodium Valproate Injection therapy should then be gradual, with target dose being reached after about two weeks. In certain cases it may be necessary to raise the dose by 5-10mg/kg/day when used

In the exceptional circumstances when Sodium Valproate Injection is the only available treatment option during pregnancy, you will be monitored very closely both for the management of your underlying condition and to check how your unborn child is developing. You and your partner should receive counselling and support regarding the valproate-exposed pregnancy.

Ask your doctor or nurse about taking folic acid. Folic acid can lower the general risk of *spina bifida* and early miscarriage that exists with all pregnancies. However, it is unlikely that it will reduce the risk of birth defects associated with valproate use.

Key messages:
- Schedule an urgent appointment with your doctor. Do not stop taking Sodium Valproate Injection unless your specialist tells you to
- Make sure you are referred to a specialist experienced in the treatment of epilepsy to evaluate the possibility of alternative treatment options
- You must get thorough counselling on the risks of Sodium Valproate Injection during pregnancy, including malformations and physical and mental development disorders in children
- Make sure you are referred to a specialist for prenatal monitoring to examine for potential malformations.

Make sure you read the Patient Guide that you will receive from your doctor, pharmacist or nurse. Your specialist will discuss the Annual Risk Acknowledgement Form with you and will ask you to sign it and keep it. You will also receive a Patient Card from your doctor, pharmacist or nurse to remind you of valproate risks in pregnancy.

Newborn babies of mothers who took valproate during pregnancy may have:
- Blood clotting problems (such as blood not clotting very well). This may appear as bruising or bleeding which takes a long time to stop
- Hypoglycaemia (low blood sugar)
- Hypothyroidism (underactive thyroid gland, which can cause tiredness or weight gain)
- Withdrawal syndrome (including agitation, irritability, hyperexcitability, jitteriness, hyperkinesia, muscle problems, tremor, convulsions and feeding problems). In particular, this may occur in newborns whose mothers have taken valproate during the last trimester of their pregnancy.

Breast-feeding
Very little Sodium Valproate Injection gets into breast milk. However, talk to your doctor about whether you should breast-feed your baby. Ask your doctor, pharmacist or nurse for advice before taking or having any medicine.

Important advice for male patients
Potential risks related to taking valproate in the 3 months before conception of a child
A study suggests a possible risk of mental and movement related developmental disorders (problems with early childhood development) in children born to fathers treated with valproate in the 3 months before conception. In this study, around 5 children in 100 had such disorders when born to fathers treated with valproate as compared to around 3 children in 100 when born to fathers treated with lamotrigine or levetiracetam (other medicines that can be used to treat your disease). The risk for children born to fathers who stopped valproate treatment 3 months (the time needed to form new sperm) or longer before conception is not known. The study has limitations and therefore it is not clear if the increased risk for movement and mental developmental disorders suggested by this study is caused by valproate. The study was not large enough to show which particular type of movement and mental developmental disorder children may be at risk of developing.

As a precautionary measure, your GP or specialist 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 specialist 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 taking valproate or for 3 months after stopping valproate.

Talk to your GP or specialist if you are thinking about having a baby.

If your female partner becomes pregnant while you used valproate in the 3 months period before conception and you have questions, contact your GP or specialist. Do not stop your treatment without talking to your GP or specialist. If you stop your treatment, your symptoms may become worse.

You should get regular appointments with your GP. During this visit your GP will discuss with you the precautions associated with valproate use. They will refer you to a specialist to discuss the possibility of other treatments that can be used to treat your disease, depending on your individual situation.

Driving and using machines
You may feel sleepy when taking Sodium Valproate Injection. If this happens to you, do not drive or use any tools or machines. Taking other medicines used to treat fits or calm emotional and mental health problems may increase sleepiness.

3. How Sodium Valproate Injection is given

Sodium Valproate Injection is always given to you by a doctor or nurse. This is because it needs to be given as a slow injection or infusion into the vein.

If you are not sure why you are being given Sodium Valproate Injection or have any questions about how much Sodium Valproate Injection is being given to you, speak to your doctor or nurse.

Your doctor will stop giving you Sodium Valproate Injection and change you to oral therapy (by mouth) as soon as possible.

Sodium Valproate Injection treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

How much will be given to you
- Your doctor will decide how much Sodium Valproate Injection to give you depending on your illness. The amount of Sodium Valproate Injection given to you or your child will depend on you or your child's age or body weight
- If you have been taking Sodium Valproate by mouth your doctor may decide to give you the same amount of Sodium Valproate Injection by continuous or repeated infusion.

If you have not had Sodium Valproate Injection before, the doctor will use the following doses:

Adults (including the elderly)
- The starting dose is usually 400-800mg (up to 10mg per kilogram of body weight)
- This is given as a slow intravenous injection over 3-5 minutes
- This is followed by a continuous or repeated infusion, up to a maximum of 2500mg each day.

Children
- The usual dose is 20-30mg for each kilogram of body weight each day
- This may be increased to 40mg for each kilogram of body weight each day depending on your child's illness.

Patients with kidney problems
- Your doctor may decide to adjust your or your child's dose.

Patients taking other medicines for fits (epilepsy)
- You or your child may be taking other medicines for epilepsy at the same time as Sodium Valproate Injection. If so, your doctor should gradually initiate treatment depending on yours or your child's condition
- Your doctor may increase the dose of Sodium Valproate Injection by 5-10mg for each kilogram of body weight each day depending on which other medicines you are taking.

If you have more Sodium Valproate Injection than you should
It is unlikely that your doctor or nurse will give you too much medicine. Your doctor will be checking your progress and checking the medicine that you are given. Always ask if you are not sure why you are getting a dose of medicine.

The following effects may happen: feeling sick or being sick, headache, blurred vision due to pupil of the eye becoming smaller, dizziness, poor reflexes, confusion, memory loss and tiredness. You may also have weak or 'floppy muscles', fits (seizures), loss of consciousness, behavioural changes and breathing difficulties such as fast breathing, shortness of breath or chest pain.

If you forget to have Sodium Valproate Injection
Your doctor or nurse will have instructions on when to give you this medicine. It is unlikely that you will not be given the medicine as it has been prescribed. However, if you think you may have missed a dose, then talk to your doctor or nurse.

If you stop receiving Sodium Valproate Injection
It is important for you to keep having Sodium Valproate Injection until your specialist decides to stop them. If you stop having Sodium Valproate Injection before your specialist decides to stop it, your condition may get worse.

Tests
Make sure you or your child keep your regular appointments for a check-up. They are very important as your or your child's dose may need to be changed. If you or your child go into hospital or visit another doctor or a dentist, tell them you have been given Sodium Valproate Injection.

If you have any further questions about receiving this product, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines Sodium Valproate Injection can cause side effects, although not everybody gets them. Side effects are more likely to happen at the start of treatment.

Tell your doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment:
- You have an **allergic reaction** which may manifest as:
  - o Blisters with skin detachment (blistering, peeling or bleeding on any part of your skin (including your lips, eyes, mouth, nose, genitals, hands or feet) with or without rash), sometimes with flu-like symptoms such as fever, chills, or aching muscles. These may be signs of conditions named 'Toxic epidermal necrolysis' or 'Stevens-Johnson Syndrome'
  - o Skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These may be signs of a condition named 'erythema multiforme'
  - o Allergy-triggered swelling with painful itchy welts (most often around the eyes, lips, throat and sometimes hands and feet) and swallowing or breathing problems. These may be signs of 'angioedema' or an anaphylactic reaction
  - o Syndrome with skin rash, fever, lymph node enlargement and possible impairment of other organs. These may be signs of a condition named 'Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)'.
- Liver problems and problems of the pancreas may show as a sudden illness which may happen in the first six months of treatment. This happens in a very small number of people having Sodium Valproate Injection. It includes feeling sick (nausea) and being sick (vomiting) many times; extreme tiredness, drowsiness and weakness; stomach pain including severe upper stomach pain; yellowing of the skin or whites of the eyes (jaundice); loss of appetite; swelling of the legs and feet (may also include other parts of the body); worsening of your fits or a general feeling of being unwell. Your doctor may stop giving you Sodium Valproate Injection immediately if you have these symptoms
- Blood disorders that can be shown in blood tests. Signs may include:
  - o Spontaneous bruising or bleeding due to blood clotting problems or decreased platelet count, or getting more infections than usual (thrombocytopenia)
  - o Severe decrease of white blood cells or bone marrow failure, sometimes revealed by fever and breathing difficulty (agranulocytosis)
  - o Decreased red blood cell count (anaemia) or abnormally increased red blood cell size (macrocytosis)
  - o Bone marrow disorders that affect red blood cells, white blood cells and platelets (pancytopenia).
- Drowsiness, change in consciousness level (including coma), confusion, loss of memory, abnormal behaviour including changes in attention, concentration and mood. This could also be associated with hallucinations or more frequent or severe fits. This is more likely if other medicine to treat fits such as phenobarbital and topiramate are taken at the same time or if the Sodium Valproate Injection starting dose is high or has been suddenly increased
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism)
- Difficulty breathing, pain or pressure in the chest (especially when breathing in), shortness of breath and dry cough due to build-up of fluid around the lungs (pleural effusion)
- An increase in the number and severity of convulsions
- Muscle pain and weakness (rhabdomyolysis)
- Joint pain, fever, fatigue or rash. These may be signs of systemic lupus erythematosus (SLE)
- Problems with balance and co-ordination, feeling lethargic or less alert, associated with being sick (vomiting). This may be due to an increased amount of ammonia in your blood
- Shakiness (tremor), jerky muscle movements, unsteadiness when walking (parkinsonism, extrapyramidal disorder, ataxia)
- Rapid, uncontrollable movement of the eyes
- Kidney disease or kidney problems (renal failure, tubulointerstitial nephritis and Fanconi syndrome) which may manifest as reduced urinary output or blood in the urine
- Confusion, that could be due to decreased levels of sodium in your blood, identified by a blood test, or to a condition named 'Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion'.

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days, or if you notice any side effects not listed in this leaflet:
- Feeling sick (nausea), being sick (vomiting), stomach ache or diarrhoea, especially when starting treatment
- Overgrowth of gums (gingival hypertrophia), swelling of gums or mouth, sore mouth, mouth ulcers and burning feeling of mouth (stomatitis)
- Darker areas of skin and mucosae (hyperpigmentation)
- Headache
- Hearing loss, hearing problems or deafness
- Double vision
- Nail and nail bed disorders
- Skin problems such as rashes. These happen rarely, but more often in people also taking lamotrigine
- Transient hair loss, abnormal hair growth, abnormal hair texture, changes in hair colour
- Increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest (particularly in women), acne or thinning hair
- Skin rash caused by inflammation of small blood vessels (vasculitis)
- Irregularity or absence of women's period, pain during women's period, cysts in the ovaries (polycystic ovaries)
- Breast enlargement in men, male infertility (usually reversible after treatment discontinuation and may be reversible after dose reduction. Do not stop your treatment without speaking to your doctor first)
- Swelling of the feet and legs (oedema)
- Obesity, weight gain - as your appetite may be increased
- Bedwetting or increased need to pass urine, urinary incontinence (unintentional passing of urine)
- Passing a lot of urine and feeling thirsty (Fanconi syndrome)
- Decrease in carnitine levels (shown in blood or muscular tests)
- Seeing, feeling or hearing things that are not there (hallucinations)
- Aggression, agitation, disturbance in attention, abnormal behaviour, restlessness/hyperactivity, memory impairment, or cognitive or learning disorder
- Tingling or numbness in the hands and feet
- Lowering of normal body temperature.

There have been reports of bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures. Check with your doctor or pharmacist if you are on long-term anti-epileptic medication, have a history of osteoporosis, or take steroids.

Tests
Sodium Valproate Injection can change levels of liver enzymes, blood clotting factors, salts or sugars shown up on blood and urine tests.

Additional side effects in children
Some side effects of valproate occur more frequently in children or are more severe compared to adults. These include liver damage, inflammation of the pancreas (pancreatitis), bedwetting (enuresis), renal dysfunction (Fanconi Syndrome), overgrowth of gum tissue, aggression, agitation, disturbance in attention, abnormal behaviour, hyperactivity and learning disorder.

Reporting of side effects
If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sodium Valproate Injection

This medicine will be kept by your doctor or nurse out of the sight and reach of children.
Do not have this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
Do not freeze. Only clear solutions free of particles should be used.
The contents of the ampoule are for single use only.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Sodium Valproate Injection contains
The active ingredient is sodium valproate 100mg per ml.
The other ingredients are Disodium hydrogen phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate, phosphoric acid, sodium hydroxide and water for injections.

What Sodium Valproate Injection looks like and contents of the pack
Sodium Valproate Injection is a clear colourless solution. It is available in glass ampoules containing either 4ml (400mg sodium valproate) or 10ml (1000mg sodium valproate) of the solution for injection. Each pack contains 1, 5 or 10 ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder: Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK.
Manufacturers: CP Pharmaceuticals Ltd, Ash Road North, Wrexham Industrial Estate, Wrexham, LL13 9UF, UK

Steriscience Sp. z o.o.,
10 Daniszewska Street,
Warsaw, 03-230,
Poland

Other sources of information:
To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge: **0800 198 5000 (UK Only)**

Please be ready to give the following information:

Product Name	Reference number
Sodium Valproate 100mg/ml Solution for Injection or Infusion	29831/0506

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last revised in 12/2024

105857/16

WOCKHARDT

in combination with anti-convulsants which induce liver enzyme activity, e.g. phenytoin, phenobarbital and carbamazepine. Once known enzyme inducers have been withdrawn it may be possible to maintain seizure control on a reduced dose of Sodium Valproate Injection. When barbiturates are being administered concomitantly and particularly if sedation is observed (particularly in children) the dosage of barbiturate should be reduced.

Optimum dosage is mainly determined by seizure control and routine measurement of plasma levels is unnecessary. However, a method for measurement of plasma levels is available and may be helpful where there is poor control or side effects are suspected (see SmPC section 5.2).

Method of administration
Sodium Valproate Injection may be given by direct slow intravenous injection or by infusion using a separate intravenous line in normal saline, dextrose 5%, or dextrose saline.
Each vial of Sodium Valproate Injection is for single dose injection only. For instructions on preparation and dilution of Sodium Valproate Injection before administration (see section 6.6).
Sodium Valproate Injection should not be administered via the same IV line as other IV additives. The intravenous solution is suitable for infusion by PVC, polyethylene or glass containers.

Pharmaceutical Particulars
List of Excipients
Disodium hydrogen phosphate dodecahydrate
Sodium dihydrogen phosphate dihydrate
Phosphoric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

Incompatibilities
Sodium valproate Intravenous should not be administered via the same line as other IV additives. This medicinal product must not be mixed with other medicinal products except those mentioned in the section entitled 'Special precautions for disposal and other handling'.

Shelf Life
Unopened: 3 years
After dilution according to the directions detailed in the section entitled 'Special precautions for disposal and other handling': Chemical and physical in-use stability has been demonstrated for seven days at 20 - 22°C. From a microbiological point of view, the product should be used immediately after opening. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally be not longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Special Precautions for Storage
Do not freeze.

Nature and contents of container
Clear glass 5ml-capacity ampoules (PhEur Type I, One Point Cut with black spot), containing 4ml of solution and clear glass 10ml-capacity ampoules (PhEur Type I, One Point Cut with red spot) containing 10ml of solution.
The ampoules are packed in a PVC tray and cardboard box in packs of 1, 5 or 10 ampoules per pack. Not all pack sizes may be marketed.

Special precautions for disposal and other handling
For infusion the product may be diluted in 0.9% saline or 5% dextrose. Tests with the recommended infusion solutions over seven days at 20 - 22°C show compatibility.
Prior to use sodium valproate solution for injection and the diluted solution should be visually inspected. Only clear solutions without particles should be used.
The contents of the ampoule are for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

Marketing Authorisation Holder:
Wockhardt UK Ltd
Ash Road North
Wrexham
LL13 9UF
UK

Marketing Authorisation Number: PL 29831/0506
Date of Revision of Text: 12/2024

105857/16

WOCKHARDT