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 child when taken during pregnancy.
If you are a female able to have a baby you must use effective method of birth control (contraception) 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 if you want to become pregnant or if you think you are pregnant.
Do not stop taking Sodium Valproate Injection unless your doctor 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 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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms seem the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. 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
2. What you need to know before you are given Sodium Valproate Injection
3. How Sodium Valproate Injection is given
4. Possible side effects
5. How to store Sodium Valproate Injection
6. Contents of the pack and other information

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 see 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
- you have a rare illness called porphyria.
- you have a genetic problem caused by a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
- 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 effective method of birth control (contraception) 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 doctor. Your doctor 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 or nurse before having Sodium Valproate Injection.

Warnings and precautions
- 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 antiepileptic drugs, convulsions may become worse or happen more frequently whilst taking this medicine. If this happens contact your doctor immediately.

Talk to your doctor, nurse or pharmacist before taking Sodium Valproate Injection if:
- you have diabetes. This medicine may affect the results of urine tests
- you have a carnitine palmitoyltransferase (CPT) type II deficiency
- you have kidney problems. Your doctor may give you a lower dose
- you have fits (epilepsy), brain disease or a metabolic condition affecting your brain
- you have a 'urea cycle disorder' where too much ammonia builds up in the body
- you have an illness called 'systemic lupus erythematosus (SLE)' – a disease of the immune system which affects skin, bones, joints and internal organs
- you know that there is a genetic problem caused by a mitochondrial disorder in your family.

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

Weight gain
Having Sodium Valproate Injection 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 having Sodium Valproate Injection and during your treatment.

Other medicines and Sodium Valproate Injection
Please tell your doctor, nurse or pharmacist if you are taking or have recently taken 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 work.

The following medicines can increase the chance of you getting side effects, when taken with Sodium Valproate Injection:
- Some medicines used for pain and inflammation (salicylates) such as aspirin
- 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

Sodium Valproate Injection may increase the effect of the following medicines:
- Medicines used for thinning the blood (such as warfarin)
- Zidovudine used to treat HIV infection.
- Temozolomide used to treat cancer
- Medicines for depression
- Monoamine oxidase inhibitors (MAOI) such as moclobemide, selegiline, linezolid
- Medicines used to calm emotional and mental conditions (including schizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine
- Nimodipine
- Propofol – used for anaesthesia.

The following medicines can affect the way Sodium Valproate Injection works:
- Oestrogen-containing products (including some birth control pills).
- Some medicines used for the prevention and treatment of malaria such as mefloquine and chloroquine
- Cimetidine used for stomach ulcers
- Protease inhibitors such as lopinavir and ritonavir – used for HIV infection and AIDS
- Carbapenem agents (antibiotics used to treat bacterial infections) such as 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.
- Cholestyramine used to lower blood fat (cholesterol) levels.

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 nothing else works for you.
- If you are a woman able to have a baby, you must not take Sodium Valproate Injection unless you use effective method of birth control (contraception) 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 doctor. Your doctor 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.
- It can cause serious birth defects and can affect the way in which the child develops as it grows. Birth defects which have been reported 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. Hearing problems or deafness have been reported in children exposed to valproate during pregnancy.
- 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 10 babies in every 100 will have birth defects. This compares to 2 to 3 babies in every 100 born to women who don't have epilepsy.
- It is estimated that up to 30-40% of preschool 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.
- Autistic spectrum disorders are more often diagnosed in children exposed to valproate and there is some evidence children may be more likely to develop symptoms of Attention Deficit Hyperactivity Disorder (ADHD).
- Before prescribing this medicine to you, your doctor will have explained what might happen to your baby if you become pregnant whilst taking valproate. If you decide later you want to have a baby you must not stop taking your medicine or your method of contraception until you have discussed this with your doctor.
- If you are a parent or a caregiver of a female child treated with valproate, you should contact the 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 about taking folic acid when trying for 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:
- ○ I AM STARTING TREATMENT WITH SODIUM VALPROATE INJECTION
- ○ I AM TAKING SODIUM VALPROATE INJECTION AND NOT PLANNING TO HAVE A BABY
- ○ I AM TAKING SODIUM VALPROATE INJECTION AND PLANNING TO HAVE A BABY
- ○ 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 doctor will have explained the risks to an unborn child if you become pregnant. Once you are able to have a baby, you will need to make sure you use an effective method of birth control (contraception) without interruption throughout your 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 doctor.
- You must use an effective method of birth control (contraception) during your entire treatment with Sodium Valproate Injection.
- You must discuss the appropriate 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 doctor will make sure you are well aware and have understood all the risks and advices 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 make sure you are using an effective method of contraception without interruption 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) during your entire treatment with Sodium Valproate Injection.
- You must discuss 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.
- You must get regular (at least annual) appointments with a specialist experienced in the management of epilepsy. During this visit your doctor will make sure you are well aware and have understood all the risks and advices 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 doctor. 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 which can be seriously debilitating. Your doctor will refer you to a specialist experienced in the management of epilepsy, so that alternative treatment options can be 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 or 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 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 doctor tells you to.
- Do not stop using your birth control (contraception) before you have talked to your doctor and worked together on a plan to ensure your condition is controlled and the risks to your baby are reduced.
- First schedule an appointment with your doctor. During this visit your doctor will make sure you are well aware and have understood all the risks and advices related to the use of valproate during pregnancy.
- Your doctor 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.

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 100 mg sodium valproate. Each 4 ml ampoule contains 400 mg sodium valproate. Each 10 ml ampoule contains 1000 mg 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
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.
Posology
Dosage requirements vary according to age and body weight. 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. Special precautions for disposal and other handling of the SmPC.
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 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.
Sodium valproate injection should be replaced by oral valproate therapy as soon as practicable.
Use with Children: Daily requirement for children is usually in the range 20 – 30mg/kg body weight per day and method of administration is as above. Where adequate control is not achieved within this range, the dose may be increased to 40 mg/kg/day but only in patients in whom plasma valproic acid levels can be monitored. Above 40 mg/kg/day clinical chemistry and haematological parameters should be monitored.
Use in 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.
In patients with renal insufficiency: It may be necessary to decrease the dosage. Dosage should be adjusted according to clinical monitoring since monitoring of plasma concentrations may be misleading (see section 5.2 Pharmacokinetic Properties of the SmPC).
In patients with hepatic insufficiency: Salicylates should not be used concomitantly with sodium valproate since they employ the same metabolic pathway (see section 4.4 Special Warnings and Precautions for Use and 4.8 Undesirable Effects of the SmPC).
Liver dysfunction, including hepatic failure resulting in fatalities, has occurred in patients whose treatment included valproic acid (see section 4.3 Contraindications and 4.4 Special Warnings and Precautions for Use of the SmPC).
Salicylates should not be used in children under 16 years (see aspirin/ salicylate product information on Reye's syndrome). In addition in conjunction with sodium valproate, concomitant use in children under 3 years can increase the risk of liver toxicity (see section 4.4 Special Warnings of the SmPC).
Female children and women of childbearing potential: Valproate injection 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 sections 4.3, 4.4 and 4.6). Valproate is prescribed and dispensed according to the Valproate Pregnancy Prevention Programme (see sections 4.4 and 4.4). The benefits and risks should be carefully reconsidered at regular treatment reviews (see 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.
Combined Therapy: When starting sodium valproate injection in patients already on other anticonvulsants these should be tapered

I AM PREGNANT AND I AM USING SODIUM VALPROATE INJECTION

Do not stop taking Sodium Valproate Injection, unless your doctor 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 which can be seriously debilitating. You will be referred to a specialist experienced in the management of epilepsy, so that alternative treatment options can be evaluated.

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 could receive counselling and support regarding the valproate exposed pregnancy.

Ask your doctor 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 if you are pregnant or think you might be pregnant.
- Do not stop taking Sodium Valproate Injection unless your doctor tells you to.
- Make sure you are referred to a specialist experienced in the treatment of epilepsy to evaluate the need for alternative treatment options.
- You must get thorough counselling on the risks of Sodium Valproate Injection during pregnancy, including teratogenicity and developmental effects in children.
- Make sure you are referred to a specialist for prenatal monitoring in order to detect possible occurrences of malformations.

Make sure you read the patient guide that you will receive from your doctor. Your doctor will discuss the Annual Risk Acknowledgement Form and will ask you to sign it and keep it. You will also receive a Patient Card from your pharmacist 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 or nurse for advice before taking any medicine.

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 between 400mg and 800mg daily (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 dose of 2500mg each day.

Children

- The usual dose is between 20mg and 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 you or your child's condition
- Your doctor may increase the dose of Sodium Valproate Injection by 5 to 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.

Using too much Sodium Valproate Injection can lead to the following symptoms: feeling sick or being sick, pupils of the eye become smaller, dizziness, loss of consciousness, weak muscles and poor reflexes, breathing problems, headaches, fits (seizures), confusion, memory loss and unusual or inappropriate behaviour.

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 doctor decides to stop them. If you stop, your fits may come back.

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. 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. If you or your child go into hospital or visit another doctor or a dentist, tell them you are having Sodium Valproate Injection.

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

4. Possible side effects

Like all medicines Sodium Valproate Injection can cause side effects, although not everybody gets them.

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**. The signs may include: a rash, joint pain, fever (systemic lupus erythematosus), swallowing or breathing problems, swelling of your lips, face, throat or tongue. Hands, feet or genitals may also be affected. More severe allergic reactions can lead to lymph node enlargement and possible impairment of other organs.
- 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 and being sick many times, being very tired, sleepy and weak, stomach pain including very bad upper stomach pain, jaundice (yellowing of the skin or whites of the eyes), loss of appetite, swelling (especially of the legs and feet but may 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.
- You have a 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 could be signs of a serious allergy to the medicine called 'erythema multiforme.'
- Blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals. Also flu-like symptoms and fever. This may be something called '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. This may be something called 'Toxic epidermal necrolysis.'
- Bruising more easily and getting more infections than usual. This could be a blood problem called 'thrombocytopenia'. It can also be due to a fall in the number of white blood cells, bone marrow depression or another condition that affects red blood cells, white blood cells and platelets (pancytopenia) or how the blood clots.
- Blood clotting problems (bleeding for longer than normal), bruising or bleeding for no reason.
- Changes in mood, loss of memory, lack of concentration and deep loss of consciousness (coma).
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism)
- Breathing difficulty and pain due to inflammation of the lungs (pleural effusion)

Tell your doctor as soon as possible if you have any of the following side effects:

- Changes in behaviour including being very alert, and sometimes also aggressive, hyperactive and unusual or inappropriate behaviour. 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.
- Changes in the amount of ammonia in the blood. Symptoms of this condition are being sick, problems with balance and co-ordination, feeling lethargic or less alert.
- Feeling shaky (tremor), sleepy or unsteady when walking or jerky muscle movements
- Feeling tired or confused with loss of consciousness sometimes accompanied by hallucinations or fits.
- Blisters with the skin flaking away.
- Rapid, uncontrollable movement of the eyes
- An increase in the number and severity of convulsions

Tell your doctor, nurse or pharmacist if any of the following side effects gets 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
- Swelling of gums or sore mouth
- Feeling dizzy
- Fainting
- Hearing loss
- Nail and nail bed disorders
- Skin problems such as rashes. These happen rarely, but more often in people also taking lamotrigine.
- Hair disorders (changes in texture, colour or growth), hair loss which is usually temporary. When it grows back it may be more curly than before.
- 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)
- Changes in women's periods and increased hair growth in women
- Breast enlargement in men
- 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)
- Headache
- Seeing or hearing things that are not there (hallucinations)
- Aggression, agitation and disturbance in attention, abnormal behaviour, restlessness/hyperactivity and learning disorder
- Tingling or numbness of the hands or feet
- Lowering of normal body temperature
- Abnormal blood clotting factors
- Muscle pain and weakness (rhabdomyolysis)
- Double vision

Bone Disorders

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

Blood tests

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

Male fertility

Sodium Valproate Injection can be a contributing factor in male infertility.

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 national reporting systems listed below:

United Kingdom:
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard
Or search for MHRA Yellow Card in the Google Play or Apple App Store.

Malta:
ADR Reporting, Website: www.medicinesauthority.gov.mt/adrportal

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 pharmacist in a safe place where children cannot see or reach it.

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 in UK: Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Marketing Authorisation Holder in Malta: Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland

Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham Industrial Estate, Wrexham, LL13 9UF, UK

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.

For Malta, please call +44 1978 661261.

This medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom and Malta: Sodium Valproate 100mg/ml Solution for Injection or Infusion

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slowly. Initiation of sodium valproate injection therapy should then be gradual, with target dose reached after about two weeks. In certain cases it may be necessary to raise the dose by 5 to 10mg/kg/day when used in combination with anticonvulsants 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 barbiturates should be reduced.

N.B. In children requiring doses higher than 40 mg/kg/day clinical chemistry and haematological parameters should be monitored. 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 section 5.2 Pharmacokinetic Properties of the SmPC).

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.

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