

PACKAGE LEAFLET: INFORMATION FOR THE USER

Epilim® Intravenous 400 mg powder and solvent for 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.

Is this leaflet hard to see or read? Phone 01 4035600 for help

WARNING

Epilim, 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 Epilim. 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 Epilim unless your doctor tells you to as your condition may become worse.

Other sources of information

For the most up to date patient information leaflet and important safety information on this product for girls, women of childbearing potential and male patients, scan the QR code included in this leaflet and on the carton label with a smartphone. The same information is also available on the following URL: qr.epilimandme.ie

Patients should select the electronic patient information leaflet which matches the name of their medicine, the name of this medicine is stated in full at the beginning of this leaflet.



qr.epilimandme.ie

Read all of this leaflet carefully before you start taking this medicine

- 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 signs of illness are 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.

In this leaflet:

1. What Epilim Intravenous is and what it is used for
2. What you need to know before you take Epilim Intravenous
3. How to take Epilim Intravenous
4. Possible side effects
5. How to store Epilim Intravenous
6. Contents of the pack and other information

1. What Epilim Intravenous is and what it is used for

What Epilim Intravenous is

The name of your medicine is Epilim Intravenous 400 mg, powder and solvent for solution for injection or infusion (called Epilim Intravenous in this leaflet).

What Epilim Intravenous contains

Epilim Intravenous contains the active substance sodium valproate. This belongs to a group of medicines called anticonvulsants or anti-epileptic agents. It works by helping to calm the brain down.

What Epilim Intravenous is used for

Epilim Intravenous 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 take Epilim Intravenous

Do not take Epilim Intravenous:

Epilepsy

- For epilepsy, you must not use Epilim Intravenous if you are pregnant, unless nothing else works for you.
 - For epilepsy, if you are a woman able to have a baby, you must not take Epilim Intravenous unless you use effective method of birth control (contraception) during your entire treatment with Epilim Intravenous. Do not stop taking Epilim Intravenous 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”).
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- x If you are allergic (hypersensitive) to sodium valproate or any of the other ingredients of Epilim Intravenous (listed in Section 6: Further information). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
 - x If you have liver problems or you or your family have a history of liver problems
 - x If you have a rare illness called porphyria
 - x If you have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
 - x If you have a known metabolic disorder, i.e. a urea cycle disorder
 - x If you have a deficiency in carnitine (a very rare metabolic disease) that is untreated

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Epilim Intravenous.

Warnings and precautions

Take special care with Epilim Intravenous

CONTACT A DOCTOR IMMEDIATELY:

- If you or your child develops a sudden illness especially if it is within the first six months of treatment and particularly if it includes repeated vomiting, extreme tiredness, abdominal pain, drowsiness, weakness, loss of appetite, upper stomach pain, nausea, jaundice (yellowing of the skin or whites of the eyes), swelling of the legs or worsening of your epilepsy or a general feeling of being unwell. Epilim can affect the liver and pancreas (see Section 4 below).

- The risk of liver damage is increased if Epilim is taken by children under 3 years of age, in people taking other antiepileptic medicine at the same time or having other neurological or metabolic disease and severe forms of epilepsy.
- If you or your child taking Epilim 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.
- If your child is under 3 years of age, Epilim should not be administered together with acetylsalicylic acid (aspirin).
- 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 medicines, some patients may experience a worsening of their symptoms (more frequent or more severe convulsions) when taking this medicine. If this happens contact your 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.

Check with your doctor or pharmacist before taking your medicine if:

- ▲ You have diabetes. This medicine may affect the results of urine tests.
- ▲ 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 an illness called ‘systemic lupus erythematosus (SLE)’ - a disease of the immune system which affects skin, bones, joints and internal organs.
- ▲ You know or your doctor suspects that there is a genetic problem caused by 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 “urea cycle disorder” because of a risk of increased ammonia level in the blood.
- ▲ You have a rare disorder called “carnitine palmitoyl transferase 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 of age.
- ▲ You have a deficiency in carnitine and are taking carnitine.
- ▲ You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking valproate.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Epilim Intravenous.

Children and adolescents

Children and adolescents under 18 years of age:

Epilim Intravenous should not be used in children and adolescents under 18 years of age for the treatment of mania.

Other medicines and Epilim Intravenous

Tell your doctor 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. Some other medicines may influence the effects of valproate or vice versa. These include:

- Some medicines used for pain and inflammation (salicylates) such as aspirin see “Take special care with Epilim Intravenous”.
- 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, topiramate, acetazolamide, lamotrigine, rufinamide and felbamate
- Medicines containing quetiapine, which is used to treat schizophrenia or bipolar disorder
- Clozapine (to treat mental health conditions)
- Medicines used for thinning the blood (such as warfarin)
- Zidovudine - used for HIV infection
- Medicines for depression
- Monoamine oxidase inhibitors (MAOI) such as moclobemide, selegiline, linezolid
- Medicines used to calm emotional and mental conditions such as diazepam and olanzapine
- Propofol, an anaesthetic
- Nimodipine
- Some medicines used for the prevention and treatment of malaria such as mefloquine and chloroquine
- Cimetidine - used for stomach ulcers
- Colestyramine used to lower blood fat (cholesterol) levels
- Some medicines used for infections (antibiotics) such as rifampicin and erythromycin
- Lopinavir and ritonavir – used for HIV treatment
- Carbapenem agents (antibiotics used to treat bacterial infections)
- Estrogen-containing products (including some birth control pills)
- Metamizole – used to treat pain and fever
- Cannabidiol (used to treat epilepsy and other conditions)
- Methotrexate (used to treat cancer and inflammatory diseases)
- Some anti-infectives that contain pivalate (e.g pivampicillin, adefovir dipivoxil)

Epilim Intravenous with alcohol

Alcohol intake is not recommended during treatment.

Weight gain

Taking Epilim Intravenous 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 taking Epilim Intravenous and during your treatment. Blood tests may be required if you are to have surgery, or if you are experiencing unexplained bruising or bleeding.

Pregnancy, breast-feeding and fertility

Important advice for women

You must not stop taking Epilim Intravenous or interrupt your contraception, until you have discussed this with your doctor. Your doctor will advise you further.

Epilepsy

- For epilepsy, you must not use Epilim Intravenous if you are pregnant, unless nothing else works for you.
- For epilepsy, if you are a woman able to have a baby, you must not take Epilim Intravenous unless you use effective method of birth control (contraception) during your entire treatment with Epilim Intravenous. Do not stop taking Epilim Intravenous or your contraception, until you have discussed this with your doctor. Your doctor will advise you further

The risks of valproate when taken during pregnancy (irrespective of the disease for which valproate is used)

- 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. 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.
- 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 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 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 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 child 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 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 contraception (birth control) 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.
- There may be blood clotting problems, such as blood not clotting very well which 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) in newborns of mothers who have taken valproate during pregnancy.

- There may be a withdrawal syndrome (including agitation, irritability, hyperexcitability, jitteriness, excessive restlessness and uncontrollable movements (hyperkinesia), muscle problems, tremor, convulsions and feeding problems) in newborns of mothers who have taken valproate during the last trimester of their pregnancy.

Please choose and read the situations which apply to you from the situations described below:

- **I AM STARTING TREATMENT WITH EPILIM INTRAVENOUS**
- **I AM TAKING EPILIM INTRAVENOUS AND NOT PLANNING TO HAVE A BABY**
- **I AM TAKING EPILIM INTRAVENOUS AND PLANNING TO HAVE A BABY**
- **I AM PREGNANT AND I AM TAKING EPILIM INTRAVENOUS**

I AM STARTING TREATMENT WITH EPILIM INTRAVENOUS

If this is the first time you have been prescribed Epilim Intravenous 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 contraception without interruption throughout your treatment with Epilim Intravenous. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- Pregnancy must be excluded before start of treatment with Epilim Intravenous 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 Epilim Intravenous.
- 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.
- 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 EPILIM INTRAVENOUS 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 during your entire treatment with Epilim Intravenous. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- You must use an effective method of birth control (contraception) during your entire treatment with Epilim Intravenous.

- You must discuss contraception (birth control) 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 EPILIM INTRAVENOUS 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 Epilim Intravenous or your 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 Epilim Intravenous or switch you to another medicine or stop treatment with Epilim Intravenous 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 Epilim Intravenous unless your doctor tells you to.
- Do not stop using your methods of 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 Epilim Intravenous a long time before you become pregnant.
- Schedule an urgent appointment with your doctor if you are or think you might be pregnant.

I AM PREGNANT AND I AM TAKING EPILIM INTRAVENOUS

Do not stop taking Epilim Intravenous, 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 Epilim Intravenous 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 Epilim Intravenous 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 Epilim Intravenous during pregnancy, including teratogenicity (birth defects) and physical and mental development disorders 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.

Breast-feeding

Very little Epilim Intravenous gets into the breast milk. However, talk to your doctor about whether you should breast-feed your baby. Ask your doctor or pharmacist for advice before taking 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 movement and mental 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 doctor will discuss with you:

- The potential risk in children born to fathers treated with valproate
- The need to consider 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 taking valproate and for 3 months after stopping valproate.

Talk to your doctor 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 doctor. Do not stop your treatment without talking to your doctor. If you stop your treatment, your symptoms may become worse.

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

Make sure you read the patient guide that you will receive from your doctor. You will also receive a Patient Card from your pharmacist to remind you of the potential risks of valproate.

Driving and using machines

You may feel sleepy when taking Epilim Intravenous. 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.

Epilim Intravenous contains sodium

This medicine contains 55 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to less than 3% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to take Epilim Intravenous

Female children and women of childbearing potential

Epilim Intravenous treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

Male patients

It is recommended that Epilim Intravenous is initiated and supervised by a specialist experienced in the management of epilepsy – see section 2 Important advice for male patients.

Epilim Intravenous 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 Epilim Intravenous

or have any questions about how much Epilim Intravenous is being given to you, speak to your doctor or nurse.

Your doctor will stop giving you Epilim Intravenous and change you to Epilim tablets, granules, syrup or liquid as soon as possible. Epilim 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 to give you depending on your illness. The amount of Epilim given to you or your child will depend on you or your child's age or body weight
- If you have been taking Epilim by mouth your doctor may decide to give you the same amount of Epilim Intravenous by continuous or repeated infusion.

If you have not had Epilim before, the doctor will use the following doses:

Adults (including the elderly)

- The starting dose is usually between 400 mg and 800 mg (up to 10 mg 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 2500 mg each day

Children

- The usual dose is between 20 mg and 30 mg for each kilogram of body weight each day
- This may be increased to 40 mg 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 Epilim Intravenous. If so, your doctor should gradually initiate treatment depending on your or your child's condition
- Your doctor may increase the dose of Epilim Intravenous by 5 to 10 mg for each kilogram of body weight each day depending on which other medicines you are taking

If you take more Epilim 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 Epilim Intravenous 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, low blood pressure and unusual or inappropriate behaviour.

Taking too much Epilim may result in too much sodium in your blood (hypernatraemia).

If you forget to take Epilim Intravenous

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 taking Epilim Intravenous

It is important for you to keep having Epilim injections 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. Epilim 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 taking Epilim.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Epilim Intravenous can cause side effects, although not everybody gets them.

Contact a doctor immediately if you notice any of the following serious side effects - you may need urgent medical attention:

- You have an allergic reaction which may manifest as:
 - Blisters with skin detachment (blistering, peeling or bleeding on any part of your skin (including you lips, eyes, mouth, nose, genitals, hands or feet) with or without a rash, with sometimes flu-like symptoms such as fever, chills or aching muscle – these may be signs of conditions named 'toxic epidermal necrolysis' or 'Stevens Johnson syndrome'. These may happen more often in people also taking lamotrigine.
 - 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'.
 - An allergy triggered swelling with painful itchy welts (most often around the eyes, lips, throat and sometimes hands and feet) – these may be signs of 'angioedema'.
 - Syndrome with skin rash, fever, lymph node enlargement and possible impairment of other organs – these may be signs of a condition named 'DRESS' or Drug Rash with Eosinophilia and Systemic Symptoms.
- Problems with balance and co-ordination, feeling lethargic or less alert, associated with vomiting. This may be due to increased amount of ammonia in your blood.
- Repeated vomiting, extreme tiredness, abdominal pain, drowsiness, weakness or loss of appetite, severe upper stomach pain, nausea, jaundice (yellowing of the skin or whites of the eyes), swelling of the legs or worsening of your epilepsy or a general feeling of being unwell. These may be signs of severe liver or pancreas disorders (see Section 2 above).
- Drowsiness, changes in consciousness level (including coma), confusion, sluggishness or abnormal behaviour and memory loss, associated or not with more frequent or more severe fits, particularly if phenobarbital and topiramate are taken at the same time or if Epilim dose has been suddenly increased.
- Confusion, that could be due to decreased levels of sodium in your blood or to a condition named 'SIADH' or Syndrome of Inappropriate Antidiuretic Hormone secretion.
- An increase in the number and severity of convulsions.
- Spontaneous bruising or bleeding, due to blood clotting problems shown in blood tests.
- Severe decrease of white blood cells or bone marrow failure shown in blood tests, sometimes revealed by fever and breathing difficulty, getting more infections than usual.
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism).
- Joint pain, fever, fatigue, rash. These may be signs of systemic lupus erythematosus.
- Shakiness (tremor), uncontrollable muscle contractions, unsteadiness when walking (parkinsonism, extrapyramidal disorder, ataxia).
- Muscle pain and muscle weakness (rhabdomyolysis).
- Difficulty breathing, pain or pressure in the chest (especially when breathing in), shortness of breath and dry cough due to buildup of fluid around the lungs (pleural effusion).
- Kidney disease (renal failure, tubulointerstitial nephritis), which may manifest as reduced urinary output, loss of appetite, feeling and being sick, fits or loss of consciousness.

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days; you may need medical treatment, or if you notice any side effects not listed in this leaflet:

Very common (may affect more than 1 in 10 people):

- Nausea

Common (may affect up to 1 in 10 people):

- Decreased platelet count or decreased red blood cell count or abnormally increased red blood cell size, or bone marrow disorders (shown in blood tests)
- Weight gain, obesity
- Seeing, feeling or hearing things that are not there (hallucinations)
- Headache
- Rapid, uncontrollable movement of the eyes
- Hearing problems or deafness
- Vomiting, stomach ache, diarrhoea especially when starting the treatment, see section 2 “How to take this medicine”
- Gingival problems (mainly hypertrophy (overgrowth of gums))
- Sore mouth, swollen mouth, mouth ulcers and burning feeling of mouth (stomatitis)
- Transient hair loss, nail and nail bed disorders
- Urinary incontinence (unintentional passing of urine)
- Pain during women’s period

Uncommon (may affect up to 1 in 100 people):

- Tingling or numbness of the hands or feet
- Inflammation of small blood vessels (vasculitis)
- Skin reactions, such as rashes.
- Abnormal hair growth, abnormal hair texture, changes in hair colour
- Excessive hairiness, particularly in women, male pattern hair growth (virilism), acne (hyperandrogenism)
- Bone disorders. 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 any long-term antiepileptic medication, have a history of osteoporosis, or take steroids.
- Irregular or absence of women’s period
- Swelling of the feet and legs (oedema)
- Decrease in body temperature

Rare (may affect up to 1 in 1000 people):

- Aggression, agitation, disturbance in attention, abnormal behaviour and psychomotor hyperactivity
- Learning disorder
- Memory impairment and cognitive disorders
- Double vision
- Bedwetting or increased need to pass urine
- Passing a lot of urine and feeling thirsty (Fanconi syndrome)
- Male infertility is usually reversible after treatment discontinuation and may be reversible after dose reduction. Do not stop your treatment without speaking to your doctor first.
- Cysts in the ovaries (polycystic ovaries)

- Reduced body levels of Vitamin B8 (biotin deficiency), symptoms include a rash occurring around the eyes, nose and mouth, weak brittle nails, hair loss, loss of appetite, nausea, feeling depressed or having hallucinations

Very rare (may affect up to 1 in 10,000 people):

- Breast enlargement in men

Not known (frequency cannot be estimated from the available data):

- Decrease in carnitine levels (shown in blood or muscular tests)
- Darker areas of skin and mucosae (hyperpigmentation)

Blood tests

Epilim Intravenous 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), 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

In Ireland:

HPRA Pharmacovigilance. Website: www.hpra.ie.

In 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 Epilim Intravenous

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial and carton after EXP. The expiry date refers to the last day of that month.

Unopened vial of powder: does not require any special storage conditions.

After reconstitution: immediate use is recommended. Only clear solutions free of particles should be used.

Once prepared, Epilim Intravenous may be given:

- By intravenous injection - it should be used immediately, and any unused portion thrown away, or
- By intravenous infusion - if prepared aseptically it may be kept for up to 24 hours at 2 to 8 °C; any remaining solution should be thrown away after 24 hours. If aseptic preparation cannot be guaranteed, the solution should be used immediately.

Do not throw away any medicines via wastewater or household waste. Ask your doctor or nurse how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Epilim Intravenous contains

Each vial of powder contains 400 mg sodium valproate.

After reconstitution, each 1 ml of solution contains 100 mg sodium valproate.

What Epilim Intravenous looks like and contents of the pack

Epilim Intravenous is an off-white powder. The solvent is a clear, colourless liquid.

Epilim Intravenous is available in packs containing one vial of powder and one ampoule of solvent.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

In Ireland:

sanofi-aventis Ireland Ltd., T/A SANOFI

Citywest Business Campus

Dublin 24

Ireland

Tel: 00 353 1 4035600

Fax: 00 353 1 4035687

email: IEmedinfo@sanofi.com

In Malta:

Sanofi S.r.l.

Viale Luigi Bodio 37/b, 20158 Milan, (Italy)

Manufacturer

Sanofi S.r.l

Via Valcanello, 4

03012 Anagni

Italy

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This leaflet was last revised in April 2025.

The following information is intended for healthcare professionals only.

The vial and ampoule contain an overfill that allows withdrawal of the labelled amount:

- Vial: 415 mg of freeze-dried sodium valproate powder (displacement factor: 8.65%).
- Ampoule: 4.25 ml of solvent water for injections.

Reconstitution

- Use a graduated syringe to withdraw 3.8 ml of solvent water for injection from the ampoule and inject into the vial of freeze-dried powder.
- Allow to dissolve completely.
- The total volume of the reconstituted solution is 4.15 ml with a concentration of 100 mg/ml.
- 4 ml of the reconstituted solution for injection (100 mg/ml) can be withdrawn from the vial.

The reconstituted solution is clear and almost colourless.

Dilution

Epilim Intravenous may be given by infusion using a separate intravenous line in normal saline, dextrose 5% or dextrose saline.

The intravenous solution is suitable for infusion in PVC, polyethylene or glass containers.

Epilim Intravenous must be reconstituted immediately prior to use. Infusion solutions containing medicinal product must be used within 24 hours.