For professional information text, scan QR code on carton or visit https://www.sanofi.co.za/en/healthcare-solution/cns/epilepsy/professionalinformation/Epilim-PI

PATIENT INFORMATION LEAFLET

EPILIM can seriously harm an unborn child when taken during pregnancy. It can cause serious birth defects to body organs and/or body structures as well as harm the developing brain of the fetus and can also affect the way in which the child develops as it grows. Children whose mothers took EPILIM during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, be intellectually less able than other children, and have difficulties with language and memory.

Children whose mothers took EPILIM during pregnancy have an increased risk of developing autistic spectrum disorders, childhood autism and attention-deficit hyperactivity disorder (ADHD).

EPILIM treatment must be started and supervised by a doctor experienced in the treatment of epilepsy or bipolar disorder. You must not take EPILIM if the risk minimisation measures (Pregnancy Prevention Programme) have not been explained to you and if you cannot commit to follow the pregnancy risk minimisation measures.

SCHEDULING STATUS

S3 EPILIM INTRAVENOUS

S1 Water for Injection – EPILIM

EPILIM® INTRAVENOUS powder for solution for injection/infusion:

Each vial contains 400 mg of sodium valproate.

Water for Injection – EPILIM solvent for solution for injection/infusion:

Each ampoule contains 4 mL sterile water for injection for reconstitution.

Sugar free.

Read all of this leaflet carefully before you start receiving EPILIM INTRAVENOUS.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- EPILIM INTRAVENOUS has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What EPILIM INTRAVENOUS is and what it is used for
2. What you need to know before you or your child is given EPILIM INTRAVENOUS
3. How to receive 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

EPILIM INTRAVENOUS is used to treat epilepsy (fits). The injection is given when it is not possible to take EPILIM by mouth.

2. WHAT YOU NEED TO KNOW BEFORE YOU OR YOUR CHILD IS GIVEN EPILIM INTRAVENOUS

You or your child should not be given EPILIM INTRAVENOUS:

- If you or your child is hypersensitive (allergic) to sodium valproate (the active ingredient of EPILIM INTRAVENOUS).
- If you are breastfeeding your baby (see Pregnancy, breastfeeding and fertility).
- If you are pregnant or able to have a baby:
  - *For the treatment of epilepsy:*
    - If you or your female (girl) child is pregnant, unless there is no suitable alternative treatment (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women).
    - If you or your female (girl) child is able to have a baby, unless the conditions of the Pregnancy Prevention Programme are met (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women).
- If you or your child has an active disease of the liver, including the following:
  - If you or your child has short- or long-term (severe) hepatitis (inflammation of the liver).
  - If you or your child (or any of your close relatives) has a past history of severe hepatitis (inflammation of the liver), especially when caused by medicines.
  - If you or your child suffers from liver porphyria (a very rare metabolic disease).
- If you or your child has been told you have a genetic problem caused by a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome).
- If you or your child has a known metabolic disorder, i.e. a urea cycle disorder.
- If you have an inborn carnitine deficiency (a very rare metabolic disease) that is untreated.

If you think you or your child may have any of these problems, or if you have any doubt at all, consult your doctor before receiving EPILIM INTRAVENOUS.

Warnings and precautions

Talk to your doctor or health care provider before being given the injection:

- **If you are a woman or female adolescent able to have a baby:**
  - If you are a woman or female adolescent that is old enough to become pregnant, your doctor should only treat you with EPILIM INTRAVENOUS if you are not pregnant and you fulfil the requirements of the Pregnancy Prevention Programme (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women).
  - If you are pregnant or planning to have a baby, talk to your doctor immediately (see section 2 and Pregnancy, breastfeeding and fertility).
- 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, worsening of your epilepsy or a general feeling of being unwell, **YOU SHOULD TELL YOUR DOCTOR IMMEDIATELY**. EPILIM INTRAVENOUS can affect the liver (and sometimes the pancreas) in a very small number of patients.
- The risk of liver damage is increased if EPILIM INTRAVENOUS is administered to your child who is less than 3 years of age, and who is taking other anti-epileptic medicines at the same time or has other neurological or metabolic diseases and severe forms of epilepsy.
- Especially if your child is below 3 years of age, EPILIM INTRAVENOUS should not be administered together with acetylsalicylic acid (aspirin).
- If you or your child has systemic lupus erythematosus (SLE – a rare disease of the immune system which affects skin, bones, joints and internal organs).
- If you or your child receiving EPILIM INTRAVENOUS develops problems with balance and co-ordination, vomiting, feeling lethargic or less alert, tell your doctor immediately. This may be due to an increased amount of ammonia in your blood.

- Convulsions may become worse or happen more frequently whilst receiving EPILIM INTRAVENOUS. If this happens contact your doctor immediately.
- If you or your child has been told that you have any metabolic disorders, particularly hereditary enzyme deficiency disorders, such as a urea cycle disorder where too much ammonia builds up in the body.
- If you or your child has kidney problems. Your doctor may want to monitor the level of EPILIM INTRAVENOUS in your body or give you a lower dose.
- If you or your child puts on weight, as your appetite may be increased. Talk to your doctor about how this will affect you or your child.
- If you or your child has diabetes, EPILIM INTRAVENOUS may affect the results of urine tests.
- If at any time you or your child has thoughts of harming or killing yourselves, immediately contact your doctor.
- If you or your child drinks alcohol. Alcohol intake is not recommended during treatment with EPILIM INTRAVENOUS (see EPILIM INTRAVENOUS with food, drink and alcohol).
- If you or your child has been told that you have carnitine palmitoyl transferase type II deficiency.
- If you or your child has been told that there is a genetic problem caused by a mitochondrial disorder in your family.
- If you or your child experiences worsening of epilepsy control in terms of frequency or severity whilst receiving EPILIM INTRAVENOUS, tell your doctor immediately.
- Your doctor or your child's doctor may wish to do blood tests before you or your child starts receiving EPILIM INTRAVENOUS and during your treatment.
- EPILIM INTRAVENOUS should be used with caution in male and female children less than 18 years of age, for the treatment of epilepsy.
- EPILIM INTRAVENOUS should only be used in adult males who plan to father a child if alternative treatment options are not suitable.

Other medicines and EPILIM INTRAVENOUS

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

Some other medicines may influence the effect of EPILIM INTRAVENOUS or vice versa. These include:

- neuroleptic agents (used to treat psychological disorders) – EPILIM INTRAVENOUS may increase the effects of these medicines
- antidepressant therapy (medicines used to treat depression, including monoamine oxidase inhibitors)
- benzodiazepines, used as sleeping tablets or to treat anxiety
- other medicines used to treat epilepsy, including phenobarbital (phenobarbitone), phenytoin, primidone, lamotrigine, topiramate, carbamazepine and felbamate
- cannabidiol (used to treat epilepsy and other conditions)
- zidovudine (used to treat HIV infections and AIDS)
- mefloquine and chloroquine (used to treat or prevent malaria) may increase the likelihood of a fit. Before travelling to a malaria area, you should get advice from your or your child's doctor or pharmacist on the most appropriate tablets for prevention.
- salicylates (aspirin), especially in children below 3 years of age (see Warnings and precautions)
- anticoagulants (used to prevent blood clots)
- cimetidine (used to treat ulcers)
- erythromycin, rifampicin, linezolid (used to treat infections)
- carbapenem antibiotics such as imipenem, ertapenem and meropenem (antibiotics used to treat bacterial infections). The combination of EPILIM INTRAVENOUS and carbapenems should be avoided because it may decrease the effect of EPILIM INTRAVENOUS.
- rufinamide (used to treat convulsions)

- colestyramine (used to treat excessive high blood lipid levels)
- protease inhibitors (used to treat HIV), such as lopinavir and ritonavir
- acetazolamide (used to treat glaucoma, seizures or brain swelling). The combination with EPILIM INTRAVENOUS may cause a build-up of ammonia in the body.
- temozolomide (used to treat cancer)
- when used in combination with olanzapine (used to treat psychiatric disorders), the following effects may occur: Neutropenia – a blood disorder leading to a reduced chance of fighting infection, dry mouth, increased appetite and weight gain, problems with speech, sleepiness or extreme tiredness.
- propofol (used for anaesthesia)
- nimodipine (used in brain bleeds)
- estrogen-containing medicines (including some birth control tablets) (see Warnings and precautions). Your doctor will monitor seizures (fits) and mood control when you or your child starts or stops taking estrogen-containing tablets.
- metamizole (used to treat pain and fever) may reduce blood levels of valproate (in EPILIM INTRAVENOUS). Blood tests or close monitoring of seizure (fits) and mood control is recommended.
- methotrexate (used to treat cancer and inflammatory diseases)
- some anti-infectives that contain pivalate (e.g. pivampicillin, adefovir dipivoxil).

These medicines and others may be affected by EPILIM INTRAVENOUS or affect how well it works. You or your child may need different amounts of medicine or may need to take different medicines. Your doctor will advise you.

EPILIM INTRAVENOUS with food, drink and alcohol

Alcohol intake is not recommended during treatment with EPILIM INTRAVENOUS (see Warnings and precautions).

Pregnancy, breastfeeding and fertility

Pregnancy

You must not receive EPILIM INTRAVENOUS if you are pregnant or breastfeeding your baby (see section 2).

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care provider for advice before receiving EPILIM INTRAVENOUS.

Important information for women and female children able to have a child, and pregnant women:

If you or your female (girl) child is pregnant, you must not receive EPILIM INTRAVENOUS, unless your doctor has determined there is no suitable alternative treatment.

If you or your female (girl) child is able to have a baby, you must not receive EPILIM

INTRAVENOUS unless the conditions of the Pregnancy Prevention Programme are met.

EPILIM INTRAVENOUS can be harmful to unborn children when received by a woman during pregnancy. EPILIM INTRAVENOUS can cause serious birth defects and can affect the way in which the child develops as it grows.

Your doctor will stop giving you EPILIM INTRAVENOUS and change you to EPILIM tablets or liquid as soon as possible. Therefore, you may need to be made aware of the EPILIM conditions of Pregnancy Prevention Programme.

The conditions of the Pregnancy Prevention Programme require that before EPILIM is prescribed for you:

- Your doctor must explain what might happen to your baby if you become pregnant while using EPILIM. You need to ensure you understand these risks.
- You will be asked to perform a pregnancy test before receiving EPILIM, or thereafter if needed. This is to make sure you are not pregnant.
- Effective birth control (contraception) will be recommended for you to avoid becoming pregnant while using EPILIM.
- Your doctor will assess your understanding of contraception and the need for contraception without interruption during the entire duration of treatment with EPILIM.
- Your doctor will review your treatment regularly (at least once a year).
- **Your doctor will ask you to read and sign an "Annual Risk Acknowledgement Form"** to make sure you are well aware and have understood all the risks related to the use of EPILIM during pregnancy and are aware and understand the recommendations to avoid becoming pregnant.
- A Patient Guide will be given to you by your doctor. **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 risks using EPILIM in pregnancy.**
- Your doctor will explain what to do if you decide later that you want to have a baby. If you are planning a baby, you must first discuss this with your doctor. You must **not** stop your EPILIM treatment or interrupt your method of contraception until you have discussed this with your doctor.
- Parents or caregivers of a female (girl) child treated with EPILIM,must contact the doctor once the female child using EPILIM experiences her first menstrual period.

Please choose the situation which applies to you or your child and read the description that follows:

- I AM STARTING TREATMENT WITH EPILIM (First prescription)
- I AM RECEIVING TREATMENT WITH EPILIM AND NOT PLANNING TO HAVE A BABY
- I AM RECEIVING TREATMENT WITH EPILIM AND PLANNING TO HAVE A BABY
- I AM PREGNANT AND I AM RECEIVING TREATMENT WITH EPILIM.

I AM STARTING TREATMENT WITH EPILIM (First prescription)

- If this is the first time you have been prescribed EPILIM, your doctor would have explained the risks to an unborn child if you become pregnant.
- If you are able to have a baby or once you are able to have a baby, you will need to make sure that you use an effective method of birth control (contraception) throughout your treatment. Talk to your doctor or family planning clinic if you need advice on birth control (contraception).
- Pregnancy must be excluded before start of treatment with EPILIM through the result of a pregnancy (blood) test, to be confirmed by your doctor.
- You must discuss appropriate methods of birth control (contraception) with your doctor. Estrogen-containing birth control pills may lower the effectiveness of EPILIM INTRAVENOUS by reducing the blood levels of valproate.
- You must make sure you use an effective method of birth control (contraception) during your entire treatment.
- You must schedule regular appointments (at least annually) with a doctor experienced in the management of epilepsy.
- Tell your doctor at once if you are pregnant or think you might be pregnant.
- Tell your doctor if you plan to become pregnant.
- It is important you contact your doctor if your female (girl) child, treated with EPILIM, experiences her first menstrual period.

I AM RECEIVING TREATMENT WITH EPILIM AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with EPILIM and you do not plan to have a baby, make sure you are using an effective method of birth control (contraception) without interruption during your entire treatment with EPILIM. Talk to your doctor or family planning clinic if you need advice on contraception.

- Make sure you are using an effective method of contraception during your entire treatment.
- You must schedule regular appointments (at least annually) with a doctor experienced in the management of epilepsy.
- Tell your doctor **immediately** if you are pregnant or think you might be pregnant.
- Tell your doctor if you plan to become pregnant.
- Parents or caregivers of a female (girl) child treated with EPILIM, must contact the doctor once the female child receiving EPILIM experiences her first menstrual period.

I AM RECEIVING EPILIM AND PLANNING TO HAVE A BABY

If you are on treatment with EPILIM and planning to have a baby, first schedule an appointment with your doctor. You should talk to your doctor a long enough time before you become pregnant so that you and your doctor can put several actions in place to ensure that your pregnancy goes as smoothly as possible, and any risks to you and your unborn child are reduced as much as possible. Your doctor may prescribe another medicine for your epilepsy which may have less risk for your baby.

- Do not stop receiving/taking EPILIM and do not stop your birth control (contraception) until you have discussed this with your doctor. Your doctor will advise you on when you can stop your contraception.
- Babies born to mothers who have been on EPILIM are at serious risk of birth defects and problems with development, which can be seriously debilitating.
- Your doctor may want to adjust your treatment and/or prescribe dietary supplements of folic acid. Folic acid may lower the risk of spina bifida (a birth defect) and early

miscarriage. However, it is unlikely that folic acid will reduce the risk of birth defects associated with EPILIM use.

- You must not stop receiving EPILIM unless your doctor agrees, as there are severe risks to yourself and your developing baby if your epilepsy is not controlled.
- If you are pregnant, or think you might be pregnant, see your doctor **immediately**.

I AM PREGNANT AND I AM RECEIVING EPILIM

Women should not become pregnant while receiving EPILIM. You should use an effective method of birth control (contraception) and consult your doctor before planning pregnancy.

- EPILIM has no effect on the efficacy of your oral contraceptive pill.
- Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant. Your doctor will advise you further.
- Do not stop using EPILIM unless your doctor tells you to as your condition may become worse. During pregnancy, should a mother suffer from a serious type of seizure, where the oxygen supply to her and her unborn baby may be cut off, the risk of death to the mother and unborn child is increased.
- Make sure you are referred to a doctor experienced in the treatment of epilepsy to re-assess your treatment options.
- You must get thorough counselling on the risks of EPILIM during pregnancy, including malformations and developmental effects in children.
- Make sure you are referred to a doctor for prenatal monitoring in order to detect possible occurrences of malformations.

The risks of EPILIM when received during pregnancy:

- EPILIM INTRAVENOUS crosses the placental barrier in humans.
- Babies born to mothers who received EPILIM during pregnancy, are at serious risk of birth defects and problems with development which can be seriously debilitating.

- It is known that in women who take EPILIM, around 10 babies in every 100 will have birth defects, as compared to 2 – 3 babies in every 100 born to women who do not have epilepsy.
- These birth defects of your developing baby include spina bifida (condition where bones of the spine are not properly developed), craniofacial defects (face and skull malformations), malformation of the limbs, heart, kidney and sexual organ malformations, hypospadias (malformation of the urethra) and multiple anomalies involving various body systems.
- Hearing problems or deafness has been reported in children exposed to EPILIM during pregnancy and monitoring for signs and symptoms of hearing loss is recommended.
- Eye malformations have been reported in children exposed to valproate, as in EPILIM, during pregnancy in association with other congenital malformations. These eye malformations may affect vision.
- Children born to mothers who receive EPILIM during pregnancy, may have impaired physical and mental development or autistic disorders. There is some evidence that children may be more likely to develop symptoms of attention-deficit hyperactivity disorder (ADHD).
- It is estimated that up to 30 to 40 % of preschool children whose mothers received EPILIM during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, less intellectually able than other children, and have difficulty with language and memory.
- It is therefore essential that you discuss your treatment with your doctor if you are thinking of becoming pregnant or tell your doctor as soon as you know you are pregnant.
- Your doctor may want to adjust your treatment and/or prescribe dietary supplements of folate.
- You must not stop receiving/taking EPILIM unless your doctor agrees, as there are severe risks to yourself and your developing baby if you have uncontrolled epilepsy.

Newborn babies of mothers who received EPILIM during pregnancy may have:

- Blood clotting problems (blood not clotting very well). This may appear as bruising, or bleeding which takes a long time to stop.
- Hypoglycaemia (low blood sugar levels).
- Hypothyroidism (underactive thyroid gland, which can cause tiredness or weight gain).
- Withdrawal syndrome (agitation, irritability, hyperexcitability, jitteriness, increased muscle movement, muscle problems, tremor, convulsions and feeding problems) when received during the last trimester of pregnancy.

Important advice for male patients able to father a child

Potential risk related to taking EPILIM in the 3 months prior to conception

A study suggests that if you take valproate in the 3 months prior to conception, your child may have a higher risk for impaired mental and/or motor development compared to children born to fathers who used lamotrigine or levetiracetam, other medicines that can be used to treat your disease. In this study, around 5 children in 100 had such disorders when born from fathers treated with valproate, as in EPILIM, and about 3 in 100 children when born from fathers treated with the other medicines. There are no data on this potential risk to children fathered more than 3 months after stopping valproate treatment (the time needed for new sperm to be formed).

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

- the potential risk when fathering a child if you are treated with EPILIM
- the need to use effective contraception (birth control) for you and your female partner during the treatment and for 3 months after stopping EPILIM
- the need to consult your doctor to discuss alternative treatment options, as soon as you are planning to father a child and before discontinuing contraception (birth control)
- to not donate sperm during treatment and for 3 months after stopping treatment.

Do not stop your treatment without talking to your doctor. If you stop your treatment, your symptoms may become worse. If your female partner becomes pregnant while you used valproate in the 3 months prior to conception, both of you should contact the doctor for counselling.

You should get regular (at least annual) appointments with your doctor. During this visit your doctor will make sure you acknowledge the risk and precautions associated with EPILIM use.

Breastfeeding

EPILIM INTRAVENOUS passes into the breast milk. You should not breastfeed your baby if you are receiving EPILIM INTRAVENOUS (see section 2).

Fertility

EPILIM can cause infertility in both men and women that may not always be reversible.

Driving and using machinery

You may feel sleepy when receiving EPILIM INTRAVENOUS. Taking other medicines used to treat fits or calm emotional and mental health problems may increase sleepiness. It is not always possible to predict to what extent EPILIM may interfere with your daily activities. If you are in a situation whereby you are exposed to driving or using tools or machines after EPILIM INTRAVENOUS treatment, be mindful of this effect.

EPILIM INTRAVENOUS contains sodium

EPILIM INTRAVENOUS contains 55,35 mg sodium (main component of cooking/table salt) per vial. This is equivalent to 2,77 % of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO RECEIVE EPILIM INTRAVENOUS

Do not share medicines prescribed for you with any other person.
You will not be expected to give yourself or your child EPILIM INTRAVENOUS. It is always given to you by a doctor or a nurse. This is because it needs to be given as an injection 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 decide on the appropriate dose and administration procedure. EPILIM INTRAVENOUS treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

Your doctor will decide how much to give you depending on your illness. The amount of EPILIM INTRAVENOUS given to you or your child will depend on your or your child’s age and body weight.

EPILIM INTRAVENOUS is usually given as a slow intravenous injection over 3 – 5 minutes which may be followed by a continuous or repeated infusion (see section 6 for reconstitution information).

Your doctor will stop giving you EPILIM INTRAVENOUS and change you to EPILIM tablets or liquid as soon as possible.

Female children, women of childbearing potential and pregnant women

Pregnant women as well as female children and women that are able to have a baby must not use EPILIM unless their doctor determined that there is no suitable alternative (see section 2).

EPILIM does not reduce the effectiveness of hormonal contraceptives. Estrogen-containing contraceptives may however increase the clearance of valproate, which may result in potentially decreased EPILIM effectiveness (see Other medicines and EPILIM INTRAVENOUS).

If you have the impression that the effect of EPILIM INTRAVENOUS is too strong or too weak, tell your doctor or pharmacist.

If you or your child receives more EPILIM INTRAVENOUS than required

It is unlikely that your doctor or nurse will give you too much medicine. However, in the event of overdosage, your doctor will manage the overdosage.

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.

Signs of overdosage or receiving too much EPILIM INTRAVENOUS include:

- Coma, poor muscle tone resulting in limpness of the body.
- Inability to breathe properly.
- Having little or no reflexes when tested using a reflex hammer.
- Constriction of the pupils – pupils become smaller.
- Metabolic acidosis – which occurs when the body produces excessive quantities of acid or the kidneys are unable to remove enough acid from the body.
- Decrease in blood pressure and subsequent shutdown of the body due to shortage of blood flow.

- Death may occur in case of a large overdose.

Symptoms in cases of overdose:

- This may vary but might include seizures, very high pressures within the skull.
- The content of sodium in EPILIM INTRAVENOUS may cause hypernatraemia (excessive sodium content in the body) when taken in excess.

If you or your child missed a dose of EPILIM INTRAVENOUS

Your doctor or nurse will have instructions on when to give you EPILIM INTRAVENOUS. It is unlikely that it will not be given to you as it has been prescribed. However, if you think you may have missed a dose, then talk to your doctor or nurse.

Effects when treatment with EPILIM INTRAVENOUS is stopped

It is important for you to keep receiving EPILIM treatment until your doctor decides to stop it. If you stop, your fits may come back.

4. POSSIBLE SIDE EFFECTS

EPILIM INTRAVENOUS can have side effects.

Not all side effects reported for EPILIM INTRAVENOUS are included in this leaflet. Should your or your child's general health worsen or if you experience any untoward effects while receiving this medicine, please consult your doctor, pharmacist or other health care provider for advice.

Tell your doctor or other health care provider immediately if you notice any of the following serious side effects:

- allergic reactions, which cause joint pain, skin rashes and fever (systemic lupus erythematosus)

- an allergy-triggered swelling with painful itchy welts (most often around the eyes, lips, tongue and throat with difficulty in breathing or swallowing, and sometimes the hands and feet) (angioedema)
- syndrome with medicine rash, fever, lymph node enlargement and possible impairment of other organs (DRESS syndrome)
- repeated vomiting, extreme tiredness, abdominal pain, drowsiness, weakness, loss of appetite, severe upper stomach pain, nausea, jaundice (yellowing of the skin or whites of the eyes), swelling of the legs, worsening of your epilepsy or a general feeling of being unwell
- severe decrease in white blood cells or bone marrow failure, sometimes revealed by fever and breathing difficulty or recurring infection
- blood clotting problems (bleeding for longer than normal)
- bruising or bleeding for no reason
- EPILIM INTRAVENOUS may also cause decreased platelet or red blood cell count (pancytopenia)
- memory impairment and cognitive disorders (changes in mood, loss of memory, lack of concentration)
- loss of consciousness (coma)
- underactive thyroid gland, which causes tiredness or weight gain (hypothyroidism)
- breathing difficulty and pain due to inflammation of the lungs (pleural effusion)
- changes in consciousness level, bizarre behaviour associated or not with more frequent or more severe fits, loss of drive, particularly if phenobarbital (phenobarbitone) and topiramate are taken at the same time or if the EPILIM INTRAVENOUS dose has been increased suddenly
- changes in the amount of ammonia in the blood. Symptoms of this condition are feeling and being sick, problems with balance and co-ordination, feeling lethargic or less alert
- confusion that may be due to decreased levels of sodium in your blood

- extrapyramidal disorder (feeling shaky [tremor], sleepy or unsteady when walking or jerky muscle movements)
- blisters with skin detachment (skin flaking away)
- rapid, uncontrollable movements of the eyes
- muscle pain and muscle weakness (rhabdomyolysis)
- an increase in the number and severity of convulsions.

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

Other side effects are:

Frequent:

- vomiting, nausea (feeling sick) or stomach ache, diarrhoea
- dizziness
- hearing problems
- headache
- hair loss; when it grows back it may be curlier than before
- hair, including body and facial hair, grows more than normally in women (polycystic ovarian syndrome)
- menstrual changes (changes in a woman's period)
- weight gain (as your appetite may be increased)
- decrease in carnitine levels (shown in blood or muscular tests)
- allergic reactions
- aggression, agitation, disturbance in attention
- tingling or numbness of the hands or feet
- gingival (gum) problems, especially overgrowth
- sore mouth, swollen mouth, mouth ulcers and burning feeling of your mouth (stomatitis).

Less frequent:

- fainting, hallucinations (seeing, feeling or hearing things that are not there)

- skin reactions such as rashes
- acne, lowered voice
- hair colour changes, nail and nail bed disorders
- swelling of the feet and legs (oedema)
- kidney problems, bedwetting or increased need to pass urine
- passing a lot of urine and feeling thirsty (Fanconi syndrome)
- abnormal behaviour, restlessness/hyperactivity and learning disorder
- impairment of fertility
- decrease in 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
- double vision.

Frequency not known:

- Pelger-Huet anomaly (an inherited blood condition, where white blood cell cores have an unusual shape and structure), which your doctor will determine with a blood test.

Children:

The safety profile of EPILIM INTRAVENOUS in children is comparable to adults, but some adverse reactions are more severe or more often observed in children. There is a particular risk of severe liver damage in infants and young children, especially under the age of 3 years. Young children are also at particular risk of pancreatitis. These risks decrease with increasing age (see Warnings and precautions). Psychiatric disorders such as aggression, agitation, disturbance in attention, abnormal behaviour, psychomotor hyperactivity and learning disorder are mainly observed in children.

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can report side effects directly to Sanofi's Pharmacovigilance Unit at za.drugsafety@sanofi.com (email) or 011 256 3700 (tel). You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of EPILIM.

5. HOW TO STORE EPILIM INTRAVENOUS

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
EPILIM INTRAVENOUS will be kept by your doctor or pharmacist in a safe place. EPILIM INTRAVENOUS and Water for Injection – EPILIM should be stored at or below 30 °C in the original package until required for use.
Protect from light.
The reconstituted solution should be used immediately, and any unused portion thrown away (see section 6 for reconstitution information).

If the reconstituted solution is further diluted for infusion and prepared aseptically it may be kept for up to 24 hours at 2 – 8 °C. Any remaining solution should be thrown away after 24 hours.

EPILIM INTRAVENOUS must not be given after the expiry date stated on the pack.

Your health care provider administering EPILIM INTRAVENOUS will dispose of any unused medicine.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What EPILIM INTRAVENOUS contains

The active substance is sodium valproate.

Excipients: None.

EPILIM INTRAVENOUS must be dissolved with the ampoule of water provided. Once prepared, it may be given by intravenous injection or by intravenous infusion (see section 5 for storage conditions for the reconstituted solution).

What EPILIM INTRAVENOUS looks like and contents of the pack

EPILIM INTRAVENOUS: Off-white, sterile, freeze-dried powder for intravenous injection/ infusion in a clear 23 mL glass vial with a slotted grey rubber stopper, secured with an aluminium collar and a plastic flip-off cap.
Water for Injection – EPILIM: 4 mL clear, colourless, aqueous solvent for re-constitution in a clear glass ampoule.

1 labelled vial of EPILIM INTRAVENOUS and 1 ampoule of Water for Injection – EPILIM are packed in a cardboard carton with a leaflet.

Holder of Certificate of Registration

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Registration numbers

EPILIM INTRAVENOUS:	Y/2.5/43
Water for Injection – EPILIM:	Y/34/156

Dates of registration

EPILIM INTRAVENOUS:	13 December 1990
Water for Injection – EPILIM:	18 June 1992.