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® CR 200 prolonged-release tablets:

Each tablet contains 133,2 mg sodium valproate and 58,0 mg valproic acid equivalent to 200 mg sodium valproate.

Sugar free.

EPILIM® CR 300 prolonged-release tablets:

Each tablet contains 199,8 mg sodium valproate and 87,0 mg valproic acid equivalent to 300 mg sodium valproate.

Sugar free.

EPILIM® CR 500 prolonged-release tablets:

Each tablet contains 333,0 mg sodium valproate and 145,0 mg valproic acid equivalent to 500 mg sodium valproate.

Sugar free.

EPILIM® 100 CRUSHABLE tablets:

Each tablet contains 100 mg sodium valproate.

Sugar free.

EPILIM® LIQUID SUGAR-FREE oral liquid:

Each 5 mL contains 200 mg sodium valproate.

Preservatives: sodium methyl parahydroxybenzoate 0,1 % *m/v* and sodium propyl parahydroxybenzoate 0,04 % *m/v*.

Contains sorbitol: 925 mg/5 mL.

Contains sweetener (sodium saccharin): 12,5 mg/5 mL.

Read all of this leaflet carefully before you start taking or are given EPILIM.

- 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 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 is and what it is used for
2. What you need to know before you take or are given EPILIM
3. How to take EPILIM

4. Possible side effects

5. How to store EPILIM

6. Contents of the pack and other information.

1. WHAT EPILIM IS AND WHAT IT IS USED FOR

EPILIM is used to treat epilepsy (fits) or used to treat bipolar disorders (severe mental illness) in adults.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE OR ARE GIVEN EPILIM

Do not take EPILIM or give EPILIM to your child:

- If you or your child is hypersensitive (allergic) to sodium valproate (the active ingredient) or any of the other ingredients of EPILIM (see section 6).
- 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).
  - *For the treatment of bipolar disorder:*
    - If you are pregnant.
    - If you are a woman able to have a baby, unless the conditions of the Pregnancy Prevention Programme are met (see 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 taking EPILIM or giving EPILIM to your child.

Warnings and precautions

Take special care with EPILIM:

- **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 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 taking EPILIM and you decide you want to start a family, talk to your doctor about this as soon as possible. Do not stop EPILIM or using birth control (contraception) until you have been able to discuss this with your doctor. You need to talk to your doctor about the risks for your baby's health while keeping your illness under control. Your doctor and you should agree on what to do with your treatment before you start trying for a baby (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women).

- **If you have a female (girl) child using EPILIM:**

  Parents or caregivers of a female (girl) child treated for epilepsy with EPILIM, must contact the

doctor once the female child using EPILIM experiences her first menstrual period.

- **If you are pregnant:**

  If you are pregnant, talk to your doctor immediately (see Do not take EPILIM or give EPILIM to your child 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 can affect the liver (and sometimes the pancreas) in a very small number of patients.
- The risk of liver damage is increased if EPILIM is taken by 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 should not be administered together with acetylsalicylic acid (aspirin).
- If you or your child taking EPILIM 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 taking EPILIM. If this happens contact your doctor immediately.
- 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 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 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 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 (see Taking EPILIM with food, drink and alcohol).
- If you or your child has been told that you have carnitine palmitoyl transferase type II deficiency.
- If you have 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 taking EPILIM, contact your doctor immediately.
- Your doctor or your child's doctor may wish to do blood tests before you or your child starts taking EPILIM and during your treatment.
- EPILIM should be used with caution in male and female children less than 18 years of age, for the treatment of epilepsy.
- EPILIM should only be used in adult males who plan to father a child if alternative treatment options are not suitable.
- EPILIM should not be used in children and adolescents under the age of 18 years for the treatment of mania associated with bipolar disorders.

Other medicines and EPILIM

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 or vice versa. These include:

- neuroleptic agents (used to treat psychological disorders) – EPILIM 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 and carbapenems should be avoided because it may decrease the effect of EPILIM.
- 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 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 or 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). Monitor seizures (fits) and mood control when you start or stop taking estrogen-containing tablets.
- metamizole (used to treat pain and fever) may reduce blood levels of valproate (in EPILIM). 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 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 with food, drink and alcohol

Alcohol intake is not recommended during treatment with EPILIM (see Take special care with EPILIM).

It is preferable to take EPILIM with or after food to reduce a feeling of sickness that may occur after taking EPILIM.

Swallow controlled-release formulation tablets whole, but do not use aerated mineral water (see section 3).

EPILIM 100 CRUSHABLE tablets may be crushed and mixed with food or drinks (see section 3).

EPILIM LIQUID SUGAR-FREE should not be diluted (see section 3).

Pregnancy, breastfeeding and fertility

Pregnancy

You must not use EPILIM 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 taking EPILIM.

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 use EPILIM, 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 use EPILIM unless the conditions of the Pregnancy Prevention Programme are met.

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

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

- Your doctor must explain what might happen to your baby if you become pregnant while taking EPILIM. You need to ensure you understand these risks.
- You will be asked to perform a pregnancy test before starting 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 taking 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 of 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 taking EPILIM 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 TAKING EPILIM AND I AM NOT PLANNING TO HAVE A BABY
- I AM TAKING EPILIM AND I AM PLANNING TO HAVE A BABY
- I AM PREGNANT AND I AM TAKING 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.

- EPILIM has no effect on the efficacy of your oral contraceptive pill.
- Some estrogen-containing birth control pills may lower valproate levels (the active ingredient of EPILIM) in your blood (see Other medicines with EPILIM).
- You must make sure you are using 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 or bipolar disorder.
- 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 TAKING EPILIM AND I AM 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 (at least annually) appointments with a doctor experienced in the management of epilepsy or bipolar disorder.
- 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 child (girl) child treated with EPILIM, must contact the doctor once the female child using EPILIM experiences her first menstrual period.

I AM TAKING EPILIM AND I AM 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 taking EPILIM or 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 taking 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 TAKING 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 taking 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. Your doctor will advise you further.
- Make sure you are referred to a doctor experienced in the treatment of epilepsy or bipolar disorder 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 taken during pregnancy:

- EPILIM crosses the placental barrier in humans.
- Babies born to mothers who are taking EPILIM, 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 take 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 took 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 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 took 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 taken 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, about 5 in 100 children 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 passes into the breast milk. You should not breastfeed your baby if you are taking EPILIM (see section 2).

Fertility

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

Driving and using machinery

EPILIM may cause drowsiness or light-headedness.
It is not always possible to predict to what extent EPILIM may interfere with your daily activities. Make sure you know how you react to EPILIM before you drive a car, operate tools or machinery, or do anything else that could be dangerous if you are drowsy or light-headed.

EPILIM LIQUID SUGAR-FREE contains sorbitol

EPILIM LIQUID SUGAR-FREE contains 925 mg sorbitol per 5 mL, which may cause gastrointestinal discomfort and may have a mild laxative effect. Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have

been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive EPILIM LIQUID SUGAR-FREE.

EPILIM contains sodium

EPILIM CR 200 contains 18,43 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 0,92 % of the recommended maximum daily dietary intake of sodium for an adult.

EPILIM CR 300 contains 27,65 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 1,38 % of the recommended maximum daily dietary intake of sodium for an adult.

EPILIM CR 500 contains 46,08 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 2,30 % of the recommended maximum daily dietary intake of sodium for an adult.

EPILIM 100 CRUSHABLE contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially sodium free.

EPILIM LIQUID SUGAR-FREE contains 29,96 mg sodium (main component of cooking/table salt) per 5 mL. This is equivalent to 1,50 % of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO TAKE EPILIM

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

Always take or give your child EPILIM exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

EPILIM treatment must be started and supervised by a doctor experienced in the treatment of epilepsy.

EPILIM CR tablets: Swallow the EPILIM CR tablets whole (do not crush or chew them), with a drink of water (not with aerated mineral water), usually with or after meals. EPILIM CR is a controlled-release formulation and can be taken once or twice daily.

EPILIM 100 CRUSHABLE: The EPILIM 100 CRUSHABLE tablets may be crushed if necessary. Take with or after meals. EPILIM 100 CRUSHABLE should be taken in 2 separate doses.

EPILIM LIQUID SUGAR-FREE: Shake the bottle before each use. EPILIM LIQUID SUGAR-FREE should not be diluted and should be taken in divided doses. Take EPILIM LIQUID SUGAR-FREE using a measuring cup. After each dose, rinse the remaining liquid in the measuring cup with water and swallow the contents to make sure you take the complete dose. The measuring cup should be washed and dried after each use.

Epilepsy

Adults

The usual dose of EPILIM is between 1 000 mg and 2 000 mg per day but may be increased to 2 500 mg per day. This quantity may be given in one dose or can be divided and given in 2 separate doses, e.g. half in the morning and half in the evening.

Children

The oral solution and crushable tablets are more suitable to give to children less than 11 years of age.

Children 20 kg *and over:*

The usual dose of EPILIM is based on the child's weight as an amount of EPILIM for each kg of body weight. The usual dose is between 20 mg and 30 mg for each kg of body weight but may be increased to 35 mg for each kg of body weight per day. This quantity may be given in one dose or can be divided and given in 2 separate doses, e.g. half in the morning and half in the evening.

Children below 20 kg:

The usual dose of EPILIM is based on the child's weight as an amount of EPILIM for each kg of body weight. The usual dose is 20 mg for each kg of body weight. This quantity should be divided and given in 2 separate doses, e.g. half in the morning and half in the evening.

EPILIM CR for the treatment of mania associated with bipolar disorders in adults

The usual initial dose is 1 000 mg/day.

Elderly patients

Your dosage will be determined by the seizure control it gives you and be recommended by your doctor.

Patients with kidney problems

Your doctor may decide to adjust your or your child's dose.

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 or the conditions for the Pregnancy Prevention Programme are met (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).

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

Make sure you keep your regular check-up appointments. They are very important, as your dosage may need to be changed.

When treatment is first started, you may be prescribed a lower dose. This is because some patients need less EPILIM than others to control their fits. Your doctor will increase the dosage until your condition is controlled. Because of this, it is very important that you follow the instructions your doctor has given you about how much to take. Blood tests may be needed.

Combined therapy

If you are taking other medicines to control your epilepsy at the same time as EPILIM CR your doctor may increase the dose of EPILIM CR by 5 mg to 10 mg for each kg of body weight per day.

If you take or your child receives more EPILIM than required

An overdose of EPILIM is dangerous. In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Signs of overdosage or taking too much of EPILIM 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 may cause hypernatraemia (excessive sodium content in the body) when taken in excess.

If you or your child missed a dose of EPILIM

If you or your child missed a dose of EPILIM, take it or give it to your child as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose.

Do not take or give your child a double dose to make up for a forgotten dose.

If you have forgotten to take or give your child several doses, immediately contact your doctor.

If you or your child stops taking or receiving EPILIM

Do not stop taking or giving your child EPILIM or alter the dose without checking with your doctor.

If you stop taking or giving your child EPILIM without your doctor's advice your condition or your child's condition may get worse.

4. POSSIBLE SIDE EFFECTS

EPILIM can have side effects.

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

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

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Store EPILIM in the original package at or below 25 °C.

Protect from light and moisture.

EPILIM may spoil if not stored properly. It is very important to keep the tablets in their protective foil until just before you take them.

Do not take or use EPILIM after the expiry date stated on the pack.

Return unused or expired medicines to your pharmacist for safe disposal.

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

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What EPILIM contains

The active substance is sodium valproate.

The other ingredients are:

EPILIM CR 200, EPILIM CR 300 and EPILIM CR 500

Ethylcellulose, hydrated silica, hypromellose and violet coat (commercial coating premix) containing: hypromellose, titanium dioxide, macrogol 400, indigo carmine aluminium lake FD&C Blue No. 2, erythrosine BS aluminium lake, iron oxide black.

EPILIM 100 CRUSHABLE

Kaolin light (natural), magnesium stearate, maize starch and hydrated colloidal silica.

EPILIM LIQUID SUGAR-FREE

Cherry flavour 740 (contains ethanol), citric acid, hydroxyethyl cellulose, sodium methyl parahydroxybenzoate 0,1 % *m/v* as preservative, Ponceau red colourant, sodium propyl parahydroxybenzoate 0,04 % *m/v* as preservative, sodium saccharin, sorbitol and purified water.

What EPILIM looks like and contents of the packs

EPILIM CR 200: Unmarked oblong, violet, film-coated tablets, nominally 13,25 x 6,75 mm.

EPILIM CR 300: Unmarked oblong, violet, film-coated tablets, nominally 15 x 7,5 mm.

EPILIM CR 500: Unmarked oblong, violet, film-coated tablets, nominally 17,25 x 9,75 mm.

EPILIM CR 200, EPILIM CR 300 and EPILIM CR 500 tablets are packed in silver aluminium foil blister strips with a leaflet into printed cardboard boxes of 56 or 100 tablets.

EPILIM 100 CRUSHABLE: Round, white, scored tablet, packed in silver aluminium foil blister strips with a leaflet into printed cardboard boxes of 100 tablets.

EPILIM LIQUID SUGAR-FREE: Red, cherry-flavoured liquid packed in amber plastic or amber glass bottles of 300 mL, with polypropylene measuring cup graduated at 2,5, 5, 10, 15 and 20 mL adaptable to the child proof cap, together with a leaflet in a printed cardboard box.

Holder of Certificate of Registration

sanofi-aventis south africa (pty) ltd

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EPILIM CR 200: 27/2.5/0322

EPILIM CR 300:	Y/2.5/286
EPILIM CR 500:	27/2.5/0323
EPILIM 100 CRUSHABLE:	27/2.5/0500
EPILIM LIQUID SUGAR-FREE:	J/2.5/148

Dates of registration

EPILIM CR 200:	29 April 1993
EPILIM CR 300:	26 March 1993
EPILIM CR 500:	05 October 1995
EPILIM 100 CRUSHABLE:	24 November 1993
EPILIM LIQUID SUGAR-FREE:	22 August 1978.