

PACKAGE LEAFLET: INFORMATION FOR THE USER

Epilim® Enteric 200mg and 500mg Gastro-resistant Coated Tablets

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.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms 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 EC is and what it is used for
2. What you need to know before you take Epilim EC
3. How to take Epilim EC
4. Possible side effects
5. How to store Epilim EC
6. Contents of the pack and other information

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

What Epilim EC is

The name of your medicine is Epilim Enteric 200mg and 500mg Gastro-resistant Coated Tablets (called Epilim EC in this leaflet). "Enteric coated" means that the tablet has a protective coating that allows it to reach the intestines (gut) without being dissolved in the stomach first. This helps it from causing a stomach upset.

What Epilim EC contains

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

What Epilim EC is used for

Epilim EC is used to treat epilepsy (fits) in adults and children.

2. What you need to know before you take Epilim EC

Do not take Epilim EC:

Epilepsy

- For epilepsy, you must not use Epilim EC 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 EC unless you use effective method of birth control (contraception) during your entire treatment with Epilim EC. Do not stop taking Epilim EC 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”).
- If you are allergic (hypersensitive) to sodium valproate or any of the other ingredients of Epilim EC (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
- If you have liver problems or you or your family have a history of liver problems
- If you have a rare illness called porphyria
- If you have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
- If you have a known metabolic disorder, i.e. a urea cycle disorder

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 EC.

Take special care with Epilim EC

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.

Children and adolescents

Children and adolescents under 18 years of age:

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

Taking with food and drink

Alcohol intake is not recommended during treatment.

Warnings and precautions

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 a 'urea cycle disorder' where too much ammonia builds up in the body
- ▲ You have an illness called 'systemic lupus erythematosus (SLE)' - a disease of the immune system which affects skin, bones, joints and internal organs
- ▲ You have an underlying condition called "Carnitine palmitoyltransferase type II deficiency" which may increase the risk of muscle damage.
- ▲ You know that there is a genetic problem causing a mitochondrial disorder in your family.

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

Some patients who take Epilim EC experience a worsening of their symptoms (more frequent or more severe convulsions). Contact your doctor immediately.

Weight gain

Taking Epilim EC 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 EC and during your treatment.

Taking Epilim EC with other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Epilim EC can affect the way some other medicines work. Also some medicines can affect the way Epilim EC works.

The following medicines can increase the chance of you getting side effects, when taken with Epilim EC:

- Some medicines used for pain and inflammation (salicylates) such as aspirin.
- Some other medicines used to treat fits (epilepsy) – see page 2, 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

Epilim EC may increase the effect of the following medicines:

- 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

The following medicines can affect the way Epilim EC works:

- 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
- Estrogen-containing products (including some birth control pills)
- In particular, tell your doctor or nurse if you are taking any of the following medicines: Carbapenem agents (antibiotics used to treat bacterial infections). The combination of valproic acid and carbapenems should be avoided because it may decrease the effect of sodium valproate.

Pregnancy, breast-feeding and fertility

Important advice for women

Epilepsy

- For epilepsy, you must not use Epilim EC 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 EC unless you use effective method of birth control (contraception) during your entire treatment with Epilim EC. Do not stop taking Epilim EC 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.
- It can cause serious birth defects and can affect the way in which the child develops as it grows. Birth defects which have been reported include *spina bifida* (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects.
- If you take valproate during pregnancy you have a higher risk than other women of having a child with birth defects that require medical treatment. Because valproate has been used for many years we know that in women

who take valproate around 10 babies in every 100 will have birth defects. This compares to 2-3 babies in every 100 born to women who don't have epilepsy.

- It is estimated that up to 30-40% of preschool children whose mothers took valproate during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, intellectually less able than other children, and have difficulty with language and memory.
- Autistic spectrum disorders are more often diagnosed in children exposed to valproate and there is some evidence children may be more likely to develop symptoms of Attention Deficit Hyperactivity Disorder (ADHD).
- Before prescribing this medicine to you, your doctor will have explained what might happen to your baby if you become pregnant whilst taking valproate. If you decide later you want to have a 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.

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

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

I AM STARTING TREATMENT WITH EPILIM EC

If this is the first time you have been prescribed Epilim EC 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 EC. 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 EC 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 EC.
- 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 EC 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 EC. 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 EC.
- 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 EC 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 EC 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 EC or switch you to another medicine or stop treatment with Epilim EC 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 EC 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 EC 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 USING EPILIM EC

Do not stop taking Epilim EC, 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 EC 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 EC 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 EC during pregnancy, including teratogenicity and developmental effects in children.
- Make sure you are referred to a specialist for prenatal monitoring in order to detect possible occurrences of malformations.

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

Breast-feeding

Very little Epilim EC 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.

Driving and using machines

You may feel sleepy when taking Epilim EC. If this happens to you, do not drive or use any tools or machines.

Taking other medicines used to treat fits or calm emotional and mental health problems may increase sleepiness.

3. How to take Epilim EC

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

Always take Epilim EC exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. Epilim EC treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

Taking this medicine

- Your doctor will decide how much Epilim EC to give you or your child depending on your or your child's body weight
- Take this medicine by mouth
- **Do not** crush or chew the tablets
- If you feel the effect of your medicine is too weak or too strong, do not change the dose yourself but ask your doctor

How to take this medicine

The dose is normally split and given half in the morning and half in the evening.

How much to take

Adults (including the elderly)

- The starting dose is 600mg daily. Your doctor will gradually increase this dose by 200mg every 3 days depending on your condition
- The usual dose is generally between 1000mg and 2000mg (20-30mg per kilogram of body weight) each day
- This may be increased to 2500mg each day depending on your illness

Children over 20 kilograms

- The starting dose should be 400mg daily. Your doctor should increase this dose depending on your child's illness
- The usual dose is then between 20mg and 30mg for each kilogram of body weight each day
- This may be further increased to 35mg for each kilogram of body weight each day depending on your child's illness

Children under 20 kilograms

- The usual dose is 20mg for each kilogram of body weight each day
- Depending on the child's condition your child's doctor may decide to increase this dose

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 EC. If so, your doctor should gradually initiate treatment depending on you or your child's condition
- Your doctor may increase the dose of Epilim EC by 5 to 10mg for each kilogram of body weight each day depending on which other medicines you are taking

If you take more Epilim EC than you should

If you take more Epilim EC than you should, tell a doctor or go to a hospital casualty department straight away.

Take the medicine pack with you. This is so the doctor knows what you have taken. The following effects may happen: 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 (hyponatraemia).

If you forget to take Epilim EC

If you forget to take a dose, take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking Epilim EC

Keep taking until your doctor tells you to stop. Do not stop taking Epilim EC just because you feel better. 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 EC 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 EC.

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 EC can cause side effects, although not everybody gets them.

Tell your doctor straight away if you notice any of the following serious side effects - you may need urgent medical treatment:

- You have an allergic reaction. The signs may include: a rash, joint pain, fever (systemic lupus erythematosus), swallowing or breathing problems, swelling of your lips, face, throat or tongue. Hands, feet or genitals may also be affected. More severe allergic reactions can lead to lymph node enlargement and possible impairment of other organs.
- Liver problems and problems of the pancreas may show as a sudden illness which may happen in the first six months of treatment. This happens in a very small number of people taking Epilim EC. It includes feeling and being sick many times, being very tired, sleepy and weak, stomach pain including very bad upper stomach pain, jaundice (yellowing of the skin or whites of the eyes), loss of appetite, swelling (especially of the legs and feet but may include other parts of the body), worsening of your fits or a general feeling of being unwell. Your doctor may tell you to stop taking Epilim EC immediately if you have these symptoms
- Kidney problems. Signs may include loss of appetite, feeling and being sick, fits or loss of consciousness
- You have a skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious allergy to the medicine called 'erythema multiforme'

- Blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals. Also flu-like symptoms and fever. This may be something called 'Stevens-Johnson syndrome'
- Severe blistering rash where layers of the skin may peel off to leave large areas of raw exposed skin over the body. Also a feeling of being generally unwell, fever, chills and aching muscles. This may be something called 'Toxic epidermal necrolysis'
- 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 antiepileptic medication, have a history of osteoporosis, or take steroids
- Bruising more easily and getting more infections than usual. This could be a blood problem called 'thrombocytopenia'. It can also be due to a fall in the number of white blood cells, bone marrow depression or another condition that affects red blood cells, white blood cells and platelets (pancytopenia) or how the blood clots
- Blood clotting problems (bleeding for longer than normal), bruising or bleeding for no reason
- Changes in mood, loss of memory, confusion, lack of concentration and deep loss of consciousness (coma)
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism)
- Breathing difficulty and pain due to inflammation of the lungs (pleural effusion)

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

- Changes in behaviour including being very alert, and sometimes also aggressive, hyper-active and unusual or inappropriate behaviour. This is more likely if other medicine to treat fits such as phenobarbital and topiramate are taken at the same time or if the Epilim EC starting dose is high or has been suddenly increased
- Changes in the amount of ammonia in the blood. Symptoms of this condition are being sick, problems with balance and co-ordination, feeling lethargic or less alert
- Feeling shaky (tremor), sleepy or unsteady when walking or jerky muscle movements
- Feeling tired or confused with loss of consciousness sometimes accompanied by hallucinations or fits
- Blisters with the skin flaking away
- Rapid, uncontrollable movement of the eyes
- If you feel depressed or have hallucinations, loss of appetite, nausea, have a rash occurring around the eyes, nose, and mouth. These could be signs of biotin deficiency

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

- Feeling sick, vomiting, red, swollen or bleeding gums, swollen mouth or lips, stomach ache or diarrhoea, especially when starting treatment. This may be helped by taking the tablets with food
- Fainting
- Nausea
- Sedation
- Extrapyrarnidal disorders
- Hearing loss
- Skin problems such as rashes. These happen rarely, but more often in people also taking lamotrigine
- Hair loss which is usually temporary. When it grows back it may be more curly than before
- Changes to hair (colour/texture/growth)
- Skin rash caused by narrow or blocked blood vessels (vasculitis)
- Changes in women's periods and increased hair growth in women, acne or excessively oily skin. Male pattern baldness in women
- Breast enlargement in men
- Male infertility
- Swelling of the feet and legs (oedema)
- Weight gain - as your appetite may be increased
- Nail and nail bed disorders
- Kidney problems, bedwetting or increased need to pass urine
- Headache
- Aggression, agitation, disturbance in attention, abnormal behaviour, restlessness, hyperactivity and learning disorder
- Tingling or numbness in the hands and feet.
- Sore muscles and darkened urine (rhabdomyolysis)
- Feeling cold, cold or pale skin, feeling listless and tired (hyperthermia)

Blood tests

Epilim EC can change levels of liver enzymes, salts or sugars shown up on blood and urine tests.

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 HPRC Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Epilim EC

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

Do not take this medicine after the expiry date shown on the blister and carton after EXP. The expiry date refers to the last day of that month.

Do not remove the tablets from the foil until just before you take them. Do not cut the blister strips. Store in a dry place. Do not store above 30°C.

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

6. Contents of the pack and other Information

What Epilim EC contains

- Each 200mg enteric coated tablet contains 200mg of the active substance, sodium valproate
- Each 500mg enteric coated tablet contains 500mg of the active substance, sodium valproate
- The other ingredients are povidone, talc, magnesium stearate, calcium silicate, polyvinyl acetate phthalate, citric acid monohydrate, hypromellose, macrogol 6000, violet lake solids (containing titanium dioxide, amaranth aluminium lake, indigo carmine aluminium lake and hydroxypropyl cellulose), diethyl phthalate and stearic acid

What Epilim EC looks like and contents of the pack

Epilim EC tablets are round and lilac coloured. The tablets are supplied in blister packs of 30, 100 or 112. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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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 August 2018