PACKAGE LEAFLET: INFORMATION FOR THE USER

Epilim® Chrono 200mg, 300mg and 500mg Prolonged Release Tablets

sodium valproate

SANOFI

▼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

Valproate can cause birth defects and problems with early development of the child if it is taken during pregnancy. If you are a female of childbearing age you should use an effective method of contraception throughout your treatment. Your doctor will discuss this with you but you should also follow the advice in section 2 of this leaflet. Tell your doctor at once if you become pregnant or think you might be pregnant.

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

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

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

What Epilim Chrono is

The name of your medicine is Epilim Chrono 200, 300 and 500mg Prolonged Release Tablets (called Epilim Chrono in this leaflet). “Prolonged release” means that the active ingredient sodium valproate is slowly released from the tablets over a period of time.

What Epilim Chrono contains

Epilim Chrono 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 Chrono is used for

Epilim Chrono is a medicine for the treatment of epilepsy and mania.

Epilim Chrono is used in the treatment of:

- Epilepsy (fits) in adults and children
- Mania, where you may feel excited, elated, agitated, enthusiastic or hyperactive. Mania occurs in an illness called “bipolar disorder”. Epilim Chrono can be used when lithium can not be used.

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

Do not take Epilim Chrono and tell your doctor if:

- You are allergic (hypersensitive) to sodium valproate or any of the other ingredients of Epilim Chrono (listed in Section 6 below). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- You have liver problems or you or your family have a history of liver problems
- You have a rare illness called porphyria
- You have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)

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 Chrono.

Take special care with Epilim Chrono

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 Chrono 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 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 Chrono.

Weight gain

Taking Epilim Chrono 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 Chrono and during your treatment.

Taking Epilim Chrono 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 Chrono can affect the way some other medicines work. Also some medicines can affect the way Epilim Chrono works.

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

- Some medicines used for pain and inflammation (salicylates) such as aspirin

- Some other medicines used to treat fits (epilepsy) – see section 3, "Patients taking other medicines for 'fits'". This includes medicines such as phenobarbital, primidone, phenytoin, carbamazepine, topiramate, lamotrigine and felbamate
- Medicines containing quetiapine, which is used to treat schizophrenia or bipolar disorder

Epilim Chrono 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

The following medicines can affect the way Epilim Chrono 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
- 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

- Valproate can be harmful to unborn children when taken by a woman during pregnancy.
- 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 ever 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).
- If you are a woman capable of becoming pregnant your doctor should only prescribe valproate for you if nothing else works for you.
- 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 should not stop taking your medicine until you have discussed this with your doctor and agreed a plan for switching you onto another product if this is possible.
- 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.

FIRST PRESCRIPTION

If this is the first time you have been prescribed valproate your doctor will have explained the risks to an unborn child if you become pregnant. Once you are of childbearing age, you will need to make sure you use an effective method of contraception throughout your treatment. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- Make sure you are using an effective method of contraception.
- Tell your doctor at once if you are pregnant or think you might be pregnant.

CONTINUING TREATMENT AND NOT TRYING FOR A BABY

If you are continuing treatment with valproate but you don't plan to have a baby make sure you are using an effective method of contraception. Talk to your doctor or family planning clinic if you need advice on contraception.

Key messages:

- Make sure you are using an effective method of contraception
- Tell your doctor at once if you are pregnant or think you might be pregnant.

CONTINUING TREATMENT AND CONSIDERING TRYING FOR A BABY

If you are continuing treatment with valproate and you are now thinking of trying for a baby you must not stop taking either your valproate or your contraceptive medicine until you have discussed this with your prescriber. You should talk to your doctor well before you become pregnant so that you 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 doctor may decide to change the dose of valproate or switch you to another medicine before you start trying for a baby.

If you do become pregnant you will be monitored very closely both for the management of your underlying condition and to check how your unborn child is developing.

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 it unlikely that it will reduce the risk of birth defects associated with valproate use.

Key messages:

- Do not stop using your contraception before you have talked to your doctor and worked together on a plan to ensure your epilepsy/bipolar disorder is controlled and the risks to your baby are reduced.
- Tell your doctor at once when you know or think you might be pregnant.

UNPLANNED PREGNANCY WHILST CONTINUING TREATMENT

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. If you are taking valproate and you think you are pregnant or might be pregnant contact your doctor at once. Do not stop taking your medicine until your doctor tells you to.

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:

- Tell your doctor at once if you know you are pregnant or think you might be pregnant.
- Do not stop taking valproate unless your doctor tells you to.

Make sure that you receive, read and understand the Patient Booklet and Information Form which will be discussed with you by your doctor.

Breast-feeding
Very little Epilim Chrono 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 Chrono. 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 Chrono

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

Taking this medicine
- Your doctor will decide how much Epilim Chrono to give you or your child depending on your or your child's body weight
- Take this medicine by mouth
- Take Epilim Chrono with or after food. This will help to stop the feelings of sickness that may happen after taking Epilim Chrono.
- **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 you doctor

How to take this medicine
- This medicine can be taken once or twice daily

How much to take

Dosage for Mania:
The daily dosage should be established and controlled individually by your doctor.

Initial dose: The recommended initial daily dose is 750mg.

Mean daily dose: The recommended daily doses usually range between 1000 mg and 2000 mg.

Dosage for Epilepsy:

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
Epilim Chrono is not recommended in children that weigh less than 20 kilograms. Epilim Liquid (sugar free) or Epilim Syrup is recommended instead

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 Chrono. If so, your doctor should gradually initiate treatment depending on you or your child's condition
- Your doctor may increase the dose of Epilim Chrono 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 Chrono than you should
If you take more Epilim Chrono 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 (hypernatraemia).

If you forget to take Epilim Chrono
If you forget to take a dose, take it as soon as you remember. However, if it 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 Chrono
Keep taking until your doctor tells you to stop. Do not stop taking Epilim Chrono 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 Chrono 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 Chrono.

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 Chrono can cause side effects, although not everybody 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 Chrono. 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 Chrono 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 Chrono 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 or by taking Epilim EC Tablets instead
- Fainting
- Nausea
- Sedation
- Extrapyramidal 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
- 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 Chrono 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 HPRA 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 Chrono

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 Chrono contains

- Each 200mg prolonged release tablet contains a mixture of 133.2mg sodium valproate and 58mg valproic acid, equivalent to 200mg of the active substance sodium valproate
- Each 300mg prolonged release tablet contains a mixture of 199.8mg sodium valproate and 87mg valproic acid, equivalent to 300mg of the active substance sodium valproate
- Each 500mg prolonged release tablet contains a mixture of 333mg sodium valproate and 145mg valproic acid, equivalent to 500mg of the active substance, sodium valproate
- The other ingredients are: hypromellose (E464), ethylcellulose, hydrated silica, titanium dioxide (E171), erythrosine BS (E127), indigo carmine (E132), iron oxide black (E172), macrogol 400

What Epilim Chrono looks like and contents of the pack

Epilim Chrono tablets are oval shaped and violet coloured. The tablets are supplied in blister packs of 100

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.

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