

PACKAGE LEAFLET: INFORMATION FOR THE USER

Epilim® Chronosphere® MR 100mg, 250mg, 500mg, 750mg & 1000mg Modified Release Granules
Sodium valproate and Valproic acid

▼ 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.

WARNING

Epilim Chronosphere, sodium valproate and valproic acid, can seriously harm an unborn baby when taken during pregnancy. If you are a female able to have a baby you must use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere. 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 Chronosphere unless your specialist tells you to as your condition may become worse.

If you are a parent or caregiver of a female child treated with Epilim Chronosphere, you must also read section 2 of this leaflet carefully and contact your child's doctor once they experience their first period.

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 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 signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

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

What Epilim Chronosphere is

The name of your medicine is Epilim Chronosphere MR 100mg, 250mg, 500mg, 750mg or 1000mg Modified Release Granules (called Epilim Chronosphere in this leaflet). "Modified release" means that the active ingredients (sodium valproate and valproic acid) are slowly released from the granules over a long period of time.

What Epilim Chronosphere contains

Epilim Chronosphere contains two medicines called sodium valproate and valproic acid. Both belong to a group of medicines called anti-convulsants or anti-epileptic agents. They work by helping to calm the brain down.

What Epilim Chronosphere is used for

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

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

Do not take Epilim Chronosphere if:

- x You are allergic (hypersensitive) to sodium valproate, valproic acid or any of the other ingredients of Epilim Chronosphere (listed in section 6). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- x You have liver problems or you and your family have a history of liver problems, especially if caused by taking a medicine.
- x You have a rare illness called porphyria which affects your metabolism.
- x You have a known metabolic disorder, i.e. a urea cycle disorder.
- x You have a genetic problem caused by a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome).
- x You are pregnant, unless nothing else works for you (see 'Pregnancy, breastfeeding and fertility – Important advice for women' below).

If you are a woman able to have a baby you must not take Epilim Chronosphere unless you use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere. Do not stop taking Epilim Chronosphere or your contraception until you have discussed this with your specialist. Your specialist will advise you further (see below under 'Pregnancy, breast-feeding and fertility – Important advice for women').

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 Chronosphere.

Warnings and precautions

- A small number of people being treated with anti-epileptics such as sodium valproate have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.
- As with other anti-epileptic drugs, convulsions may become worse or happen more frequently whilst taking this medicine. If this happens contact your doctor immediately.

Talk to your doctor or pharmacist before taking Epilim Chronosphere if:

- ▲ You have a brain disease or a metabolic condition affecting your brain.
- ▲ You have problems with your pancreas.
- ▲ You have diabetes or are being tested for diabetes. This medicine may affect the results of urine tests.
- ▲ You have a carnitine palmitoyltransferase type II deficiency.
- ▲ You have kidney problems. Your doctor may monitor your valproate level or adjust your dose.
- ▲ 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 rare disease of the immune system which affects skin, bones, joints and internal organs.
- ▲ You know that there is a genetic problem caused by 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 Chronosphere.

Weight gain

Taking Epilim Chronosphere may make you put on weight. Talk to your doctor about how this will affect you.

Blood tests

Your doctor may do blood tests and liver function tests before and during your treatment with this medicine. Epilim Chronosphere 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.

Other medicines and Epilim Chronosphere

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

In particular, check with your doctor if you are taking any of the following:

- 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, rifinamide, topiramate, acetazolamide, lamotrigine and felbamate.
 - Medicines used to calm emotional and mental health disorders (including schizizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine.
 - Monoamine oxidase inhibitors (MAOIs) such as moclobemide (used to treat depression and anxiety), selegiline (used to treat Parkinson's disease), linezolid (used to treat infections).
 - Anticoagulants such as warfarin – used to thin the blood and prevent clots.
- Your doctor may change your dose of the blood thinning medicine and monitor your treatment closely.
- Zidovudine and protease inhibitors such as lopinavir and ritonavir – used to treat HIV infection and AIDS.
 - Carbapenem agents (antibiotics used to treat bacterial infections) such as panipenem, imipenem, meropenem, rifampicin and erythromycin. The combination of Epilim Chronosphere and carbapenems should be avoided because it may decrease the effect of your medicine.
 - Some medicines used to treat or prevent malaria such as mefloquine and chloroquine.
 - Temozolomide – used to treat cancer.
 - Cimetidine – used to treat stomach ulcers.
 - Cholestyramine – used to lower blood fat (cholesterol) levels.
 - Nimodipine – used to treat bleeding in the brain (subarachnoid haemorrhage).
 - Propofol – used for anaesthesia.
 - Oestrogen-containing products (including some birth control pills).
 - Metamizole – used to treat pain and fever.

Epilim Chronosphere with alcohol

Alcohol intake is not recommended during treatment.

Pregnancy, breast-feeding and fertility

Important advice for women

- You must not use Epilim Chronosphere if you are pregnant, unless your specialist has determined that no alternative treatment works for you.
- If you are a woman able to have a baby, you must not take Epilim Chronosphere unless you use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere.
- Do not stop taking Epilim Chronosphere or your birth control (contraception), until you have discussed this with your specialist. Your specialist will advise you further.



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The risks of valproate when taken during pregnancy

- Talk to your doctor immediately if you are planning to have a baby or are pregnant.
- Valproate carries a risk if taken during pregnancy. The higher the dose, the higher the risks but all doses carry a risk, including when valproate is used in combination with other medicines to treat epilepsy.
- It can cause serious birth defects and can affect the physical and mental development of the child as it grows after birth. If you take valproate during pregnancy you have a higher risk than other women of having a child with birth defects that require medical treatment. Because valproate has been used for many years, we know that in women who take valproate around 11 babies in every 100 will have birth defects. This compares to 2-3 babies in every 100 born to women from the general population.
 - The most frequently reported birth defects include *spina bifida* (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects and multiple associated malformations affecting several organs and parts of the body. Birth defects may result in disabilities which may be severe.
 - Hearing problems or deafness have been reported in children exposed to valproate during pregnancy.
 - Eye malformations have been reported in children exposed to valproate during pregnancy in association with other congenital malformations. These eye malformations may affect vision.

- It is estimated that up to 30-40% of 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.

- Autism and related disorders are more often diagnosed in children exposed to valproate during pregnancy and there is some evidence that children exposed to valproate during pregnancy are at increased risk of developing Attention Deficit Hyperactivity Disorder (ADHD).

- Before prescribing this medicine to you, your specialist will have explained what might happen to your baby if you become pregnant whilst taking valproate.

If you decide later that you want to have a baby, you must not stop taking your medicine or your method of birth control (contraception) until you have discussed this with your specialist.

- If you are a parent or a caregiver of a female child treated with valproate, you must contact their doctor once your child using valproate experiences their first period (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 birth control (contraception) that is the most appropriate for you.
- 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.

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

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

I AM STARTING TREATMENT WITH EPILIM CHRONOSPHERE

If this is the first time you have been prescribed Epilim Chronosphere your specialist will have explained the risks to an unborn child if you become pregnant.

Once you are able to have a baby, you must use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere. Talk to your doctor or family planning clinic if you need advice on birth control (contraception).

Key messages:

- Pregnancy must be excluded before start of treatment with Epilim Chronosphere with the result of a pregnancy test, confirmed by your specialist.
- You must use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere.
- You must discuss appropriate and effective 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 (contraception).
- You must get regular (at least annual) appointments with a specialist experienced in the management of epilepsy. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice 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 CHRONOSPHERE AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with Epilim Chronosphere but you are not planning to have a baby you must use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere. Talk to your doctor or family planning clinic if you need advice on birth control (contraception).

Key messages:

- You must use an effective method of birth control (contraception) at all times during your entire treatment with Epilim Chronosphere.
- You must discuss appropriate and effective 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 (contraception).
- You must get regular (at least annual) appointments with a specialist experienced in the management of epilepsy. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice 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 CHRONOSPHERE 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 Chronosphere or your birth control (contraception) until you have discussed this with your specialist. Your specialist will advise you further.

Babies born to mothers who have been on valproate are at serious risk of birth defects and problems with development (behaviour and learning disorders), which can be seriously debilitating. Your doctor will refer you to a specialist experienced in the management of epilepsy, so that alternative treatment options are 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 Chronosphere, switch you to another medicine, or stop treatment with Epilim Chronosphere 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 Chronosphere unless your specialist tells you to.
- Do not stop using your birth control (contraception) before you have talked to your specialist and worked together on a plan to ensure your condition is controlled and the risks to you and your baby are reduced.
- First schedule an appointment with your specialist. During this visit your specialist will make sure you are well aware of and have understood all the risks and advice related to the use of valproate during pregnancy.
- Your specialist will try to switch you to another medicine or stop treatment with Epilim Chronosphere a long time before you become pregnant.
- Schedule an urgent appointment with your doctor if you are pregnant or think you might be pregnant.

I AM PREGNANT AND I AM TAKING EPILIM CHRONOSPHERE

Do not stop taking Epilim Chronosphere unless your specialist 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 (behaviour and learning disorders) 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 Chronosphere 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 should 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 Chronosphere unless your specialist tells you to.
- Make sure you are referred to a specialist experienced in the treatment of epilepsy to evaluate the possibility of alternative treatment options.

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- You must get thorough counselling on the risks of Epilim Chronosphere during pregnancy, including malformations and physical and mental development disorders in children.
- Make sure you are referred to a specialist for prenatal monitoring to examine for potential of malformations.

Make sure you read the Patient Guide that you will receive from your doctor or pharmacist. Your specialist 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.

Newborn babies of mothers who took valproate during pregnancy may have:

- Blood clotting problems (such as blood not clotting very well). This may appear as bruising or bleeding which takes a long time to stop.
- Hypoglycaemia (low blood sugar).
- Hypothyroidism (underactive thyroid gland, which can cause tiredness or weight gain).
- Withdrawal syndrome (including agitation, irritability, hyperexcitability, jitteriness, hyperkinesia, muscle problems, tremor, convulsions and feeding problems). In particular, this may occur in newborns whose mothers have taken valproate during the last trimester of their pregnancy.

Breast-feeding

Very little Epilim Chronosphere 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 Chronosphere. 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 problems may increase sleepiness.

Epilim Chronosphere contains sodium

- Epilim Chronosphere 100mg contains 9.22mg sodium (main component of cooking/table salt) in each sachet. This is equivalent to less than 1% of the recommended maximum daily dietary intake of sodium for an adult per sachet.
- Epilim Chronosphere 250mg contains 23.07mg sodium (main component of cooking/table salt) in each sachet. This is equivalent to less than 2% of the recommended maximum daily dietary intake of sodium for an adult per sachet.
- Epilim Chronosphere 500mg contains 46.08mg sodium (main component of cooking/table salt) in each sachet. This is equivalent to less than 3% of the recommended maximum daily dietary intake of sodium for an adult per sachet.
- Epilim Chronosphere 750mg contains 69.20mg sodium (main component of cooking/table salt) in each sachet. This is equivalent to less than 4% of the recommended maximum daily dietary intake of sodium for an adult per sachet.
- Epilim Chronosphere 1000mg contains 92.24mg sodium (main component of cooking/table salt) in each sachet. This is equivalent to less than 5% of the recommended maximum daily dietary intake of sodium for an adult per sachet.

3. How to take Epilim Chronosphere

Always take Epilim Chronosphere exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

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

Your doctor will decide how much Epilim Chronosphere to give you or your child depending on your or your child's body weight. 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

- Take this medicine by mouth. **Do not** crush or chew the granules.
- This medicine can be taken once or twice daily.
- The granules should be sprinkled on a small amount of soft food or drink which should be cold or at room temperature. **Do not** sprinkle Epilim Chronosphere on warm or hot foods and drinks, such as soup, coffee, tea, or something similar.
- The granules should not be given in babies bottles. This is because they can block the nipple.
- This medicine can be taken with soft food or drink such as yoghurt, mousse, jam, ice cream, milk shake and orange juice. The mixture of granules with food or drink should be swallowed immediately.
- When the granules are put onto food, you must swallow all the food with the granules to make sure you get the correct dose of medicine.
- When the granules are swallowed in a drink, the empty glass should be rinsed with a small amount of water. This water should be swallowed because some granules may stick to the glass.
- **Do not** store partially used sachets or a mixture of the granules with liquid or food for future use. Always use the full contents of each sachet.
- You may see what appears to be complete granules in your stool. This is normal as the matrix of the Epilim Chronosphere granules is not digested by the body. It does not mean that the medicine is not working.

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 1000-2000mg (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 20-30mg for each kilogram of body weight.
- This may be 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.
- 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 Chronosphere. If so, your doctor should gradually initiate treatment depending on your or your child's condition.
- Your doctor may increase the dose of Epilim Chronosphere by 5-10mg for each kilogram of body weight each day depending on which other medicines you are taking.

If you take more Epilim Chronosphere than you should

If you or your child take more Epilim Chronosphere 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, headache, blurred vision due to pupil of the eye becoming smaller, dizziness, poor reflexes, confusion, memory loss and tiredness. You may also have weak or 'floppy' muscles, fits (seizures), loss of consciousness, behavioural changes and breathing difficulties such as fast breathing, shortness of breath or chest pain.

If you forget to take Epilim Chronosphere

If you or your child 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 Chronosphere

Do not stop taking Epilim Chronosphere or alter your or your child's dose without checking with your specialist. If you or your child stop taking Epilim Chronosphere without your specialist's advice, your condition may get worse.

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. If you or your child go into hospital or visit another doctor or a dentist, tell them you are taking Epilim Chronosphere.

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 Chronosphere can cause side effects, although not everybody gets them. Side effects are more likely to happen at the start of treatment.

Tell your doctor or go to a hospital straight away if you notice any of the following serious side effects – you may need urgent medical treatment:

- You have an **allergic reaction** which may manifest as:
 - Blisters with skin detachment (blistering, peeling or bleeding on any part of your skin (including your lips, eyes, mouth, nose, genitals, hands or feet) with or without rash), sometimes with flu-like symptoms such as fever, chills, or aching muscles. These may be signs of conditions named 'toxic epidermal necrolysis' or 'Stevens-Johnson Syndrome'.
 - Skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These may be signs of a condition named 'erythema multiforme'.
 - Allergy-triggered swelling with painful itchy welts (most often around the eyes, lips, throat and sometimes hands and feet) and swallowing or breathing problems. These may be signs of 'angioedema' or an anaphylactic reaction.
 - Syndrome with skin rash, fever, lymph node enlargement and possible impairment of other organs. These may be signs of a condition named 'Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)'.
- 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 Chronosphere. It includes feeling sick (nausea) and being sick (vomiting) many times; extreme tiredness, drowsiness and weakness; stomach pain including severe upper stomach pain; yellowing of the skin or whites of the eyes (jaundice); loss of appetite; swelling of the legs and feet (may also 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 Chronosphere immediately if you have these symptoms.
- Blood disorders that can be shown in blood tests. Signs may include:
 - Spontaneous bruising or bleeding due to blood clotting problems or decreased platelet count, or getting more infections than usual (thrombocytopenia)
 - Severe decrease of white blood cells or bone marrow failure, sometimes revealed by fever and breathing difficulty (agranulocytosis)
 - Decreased red blood cell count (anaemia) or abnormally increased red blood cell size (macrocytosis)
 - Bone marrow disorders that affect red blood cells, white blood cells and platelets (pancytopenia)
- Drowsiness, change in consciousness level (including coma), confusion, loss of memory, abnormal behaviour including changes in attention, concentration and mood. This could also be associated with hallucinations or more frequent or severe fits. 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 Chronosphere starting dose is high or has been suddenly increased.
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism)
- Breathing difficulty and pain due to inflammation of the envelope of the lungs (pleural effusion)
- An increase in the number and severity of convulsions
- Muscle pain and weakness (rhabdomyolysis)
- Joint pain, fever, fatigue or rash. These may be signs of systemic lupus erythematosus (SLE).
- Problems with balance and co-ordination, feeling lethargic or less alert, associated with being sick (vomiting). This may be due to an increased amount of ammonia in your blood.
- Shakiness (tremor), jerky muscle movements, unsteadiness when walking (parkinsonism, extrapyramidal disorder, ataxia)
- Rapid, uncontrollable movement of the eyes
- Kidney disease or kidney problems (renal failure, tubulointerstitial nephritis and Fanconi syndrome) which may manifest as reduced urinary output or blood in the urine
- Confusion, that could be due to decreased levels of sodium in your blood, identified by a blood test, or to a condition named 'Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion'

- 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 (nausea), being sick (vomiting), stomachache or diarrhoea, especially when starting treatment. This may be helped by taking the tablets with food.
 - Overgrowth of gums (gingival hypertrophy), swelling of gums or mouth, sore mouth, mouth ulcers and burning feeling of mouth (stomatitis)
 - Headache
 - Hearing loss, hearing problems or deafness
 - Double vision
 - Nail and nail bed disorders
 - Skin problems such as rashes. These happen rarely, but more often in people also taking lamotrigine.
 - Transient hair loss, abnormal hair growth, abnormal hair texture, changes in hair colour
 - Increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest (particularly in women), acne or thinning hair
 - Skin rash caused by inflammation of small blood vessels (vasculitis)
 - Irregularity or absence of women's period, pain during women's period, cysts in the ovaries (polycystic ovaries)
 - Breast enlargement in men, male infertility (usually reversible after treatment discontinuation and may be reversible after dose reduction. Do not stop your treatment without speaking to your doctor first)
 - Swelling of the feet and legs (oedema)
 - Obesity, weight gain – as your appetite may be increased
 - Bedwetting or increased need to pass urine, urinary incontinence (unintentional passing of urine)
 - Seeing, feeling or hearing things that are not there (hallucinations)
 - Aggression, agitation, disturbance in attention, abnormal behaviour, restlessness/hyperactivity, memory impairment, or cognitive or learning disorder
 - Tingling or numbness in the hands and feet
 - Lowering of normal 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.

Tests
Epilim Chronosphere can change levels of liver enzymes, blood clotting factors, salts or sugars shown up on blood and urine tests.

Additional side effects in children

Some side effects of valproate occur more frequently in children or are more severe compared to adults. These include liver damage, inflammation of the pancreas (pancreatitis), bedwetting (enuresis), renal dysfunction (Fanconi Syndrome), overgrowth of gum tissue, aggression, agitation, disturbance in attention, abnormal behaviour, hyperactivity and learning disorder.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Epilim Chronosphere

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

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

Do not store above 25°C. Store in the original packaging. Do not refrigerate or freeze.

If your medicine should show any signs of deterioration, please contact your doctor or pharmacist before taking your medicine.

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 Chronosphere contains

- Each sachet of 303mg modified release granules contains a mixture of 66.66mg Sodium Valproate and 29.03mg Valproic Acid, equivalent to 100mg of the active substance Sodium Valproate.
- Each sachet of 758mg modified release granules contains a mixture of 166.76mg Sodium Valproate and 72.61mg Valproic Acid, equivalent to 250mg of the active substance Sodium Valproate.
- Each sachet of 1515mg modified release granules contains a mixture of 333.30mg Sodium Valproate and 145.14mg Valproic Acid, equivalent to 500mg of the active substance Sodium Valproate.
- Each sachet of 2273mg modified release granules contains a mixture of 500.06mg Sodium Valproate and 217.75mg Valproic Acid, equivalent to 750mg of the active substance Sodium Valproate.
- Each sachet of 3030mg modified release granules contains a mixture of 666.60mg Sodium Valproate and 290.27mg Valproic Acid, equivalent to 1000mg of the active substance Sodium Valproate.
- The other ingredients are paraffin hard, glycerol dibehenate and silica colloidal hydrated.

What Epilim Chronosphere looks like and contents of the pack

The sachets contain small off-white to slightly yellow, waxy microgranules. These modified release granules are supplied in cartons of 30 sachets.

Product Licence Holder and Manufacturer

Product Licence Holder: Mirage Pharma Ltd, Unit 6 Albion Industrial Estate, Oldbury Road, West Bromwich, B70 9BP, UK.

Manufacturer: Sanofi Winthrop Industrie, 196 Rue Du Maréchal Juin, 45200 Amilly, France

PLGB 54103/0006 - Epilim® Chronosphere® MR 100mg
 PLGB 54103/0007 - Epilim® Chronosphere® MR 250mg
 PLGB 54103/0008 - Epilim® Chronosphere® MR 500mg
 PLGB 54103/0009 - Epilim® Chronosphere® MR 750mg
 PLGB 54103/0010 - Epilim® Chronosphere® MR 1000mg

Leaflet date: 16 June 2022

Epilim and Chronosphere are trademarks of Sanofi.

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.

Other sources of information

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

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