

Depakote® 250mg and 500mg Tablets

valproic acid (as valproate semisodium)



**Is this leaflet hard to see or read?
Phone 0800 035 2525 for help.**

▼ 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

Depakote, valproate semisodium, can seriously harm an unborn child taken during pregnancy. If you are a female able to have a baby you must use an effective method of birth control (contraception) without interruption during your entire treatment with Depakote. Your doctor will discuss this with you but you should also follow the advice in section 2 of this leaflet.

Schedule an urgent appointment with your doctor if you want to become pregnant or think you are pregnant.

Do not stop taking Depakote 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, 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.

What is in this leaflet

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

1. What Depakote is and what it is used for



The name of your medicine is Depakote 250mg or 500mg Tablets (called Depakote in this leaflet). Depakote contains a medicine called valproate semisodium. This belongs to a group of medicines called mood stabilisers. It works by stabilising the levels of chemicals in your brain that affect your mood.

Depakote can be used to manage or control mania (feeling highly excited, enthusiastic, being over-active and easily irritated or distracted) caused by bipolar disorder. Bipolar disorder is where the mood changes between feeling very high (mania) and very low (depression).

Depakote can be used when lithium cannot be used.

2. What you need to know before you take Depakote



Do not take Depakote and tell your doctor if:

- X You are allergic (hypersensitive) to valproate semisodium or any of the other ingredients of Depakote (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 or your family have a history of liver problems 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 (see 'Pregnancy, breast-feeding and fertility – Important advice for women' below).



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If you are a woman able to have a baby you must not take Depakote unless you use an effective method of birth control (contraception) at all times during your treatment with Depakote. Do not stop taking Depakote 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').

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 Depakote.



Warnings and precautions

- A small number of people being treated with mood stabilisers such as valproate semisodium have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.
- In patients with epilepsy 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 Depakote if:

- ▲ You are changing from another medicine that contains valproate.
- ▲ The person taking this medicine is less than 18 years old.
- ▲ You have fits (epilepsy), 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.
- ▲ 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 the 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 Depakote.

Weight gain

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



Other medicines and Depakote

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 Depakote can affect the way some other medicines work. Also, some medicines can affect the way Depakote works.

In particular, do not take and check with your doctor if you are taking any of the following:

- Some medicines used for pain and inflammation called 'salicylates' such as aspirin.

The following medicines can affect the way Depakote works or Depakote can affect the way some of these medicines work:

- Some medicines used to treat fits (epilepsy), such as phenobarbital, primidone, phenytoin, carbamazepine, rufinamide, topiramate, acetazolamide, lamotrigine and felbamate.
Your doctor may change the dose of one of your medicines and monitor your treatment closely.
- Medicines for depression.
- Medicines used to calm emotional and mental health problems (including schizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine.
- Zidovudine and protease inhibitors such as lopinavir and ritonavir – used for HIV infection.
- Carbapenem agents (antibiotics used to treat bacterial infections) such as panipenem, imipenem, meropenem, rifampicin and erythromycin. The combination of Depakote and carbapenems should be avoided because it may decrease the effect of your medicine.
- Some medicines used for malaria such as mefloquine or chloroquine.
- Medicines used for thinning the blood such as warfarin. Your doctor may change your dose of the blood thinning medicine and monitor your treatment closely.

- Temozolomide – used for cancer.
- Cimetidine – used for stomach ulcers.
- Cholestyramine – used for lowering blood cholesterol levels.
- Nimodipine.
- Propofol – used for anaesthesia.
- Oestrogen-containing products (including some birth control pills).

Taking Depakote with food and drink

Alcohol intake is not recommended during treatment.

Pregnancy, breast-feeding and fertility

Important advice for women

- You must not use Depakote if you are pregnant.
- If you are a woman able to have a baby, you must not take Depakote, unless you use an effective method of birth control (contraception) during your entire treatment with Depakote.
- Do not stop taking Depakote or your birth control (contraception) until you have discussed this with your doctor. Your doctor will advise you further.

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.
- 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. Hearing problems or deafness have been reported in children exposed to valproate during pregnancy.
- 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 bipolar disorder.
- 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 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 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 or your method of birth control (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 their doctor once your child 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 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 the situations which apply to you and read the descriptions below:

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

I AM STARTING TREATMENT WITH DEPAKOTE

If this is the first time you have been prescribed Depakote 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 birth control (contraception) without interruption throughout your treatment with Depakote. 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 Depakote 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 Depakote.
- You must discuss 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 (contraception).
- You must get regular (at least annual) appointments with a specialist experienced in the management of bipolar disorder. During this visit your doctor 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 DEPAKOTE AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with Depakote but you don't plan to have a baby make sure you are using an effective method of birth control (contraception) without interruption during your entire treatment with Depakote. 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) during your entire treatment with Depakote.
- You must discuss 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 bipolar disorder. During this visit your doctor 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 DEPAKOTE 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 Depakote or your birth control (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 bipolar disorder 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 Depakote, switch you to another medicine, or stop treatment with Depakote a long time before you become pregnant – this is to make sure your illness is stable.

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.

Key messages:

- Do not stop taking Depakote unless your doctor tells you to.
- Do not stop using your method 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 of and have understood all the risks and advice related to the use of valproate during pregnancy.
- Your doctor will try to switch you to another medicine, or stop treatment with Depakote 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 USING DEPAKOTE

Do not stop taking Depakote, 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 bipolar disorder so that alternative treatment options can be evaluated. 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 Depakote unless your doctor tells you to.
- Make sure you are referred to a specialist experienced in the treatment of bipolar disorder to evaluate the need for alternative treatment options.
- You must get thorough counselling on the risks of Depakote during pregnancy, including malformations 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.

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

If you are breast-feeding or planning to breast-feed, talk to your doctor or pharmacist before taking any medicine.



Driving and using machines

You may feel sleepy, confused or dizzy while taking this medicine. If this happens, do not drive or use any tools or machines.

Important information about some of the ingredients of Depakote

Your medicine contains colours called 'sunset yellow aluminium lake (E110)' and 'ponceau 4R aluminium lake (E124)'. They may cause allergic reactions including asthma in some people. You are more likely to have an allergy if you are also allergic to aspirin.

3. How to take Depakote

Always take Depakote exactly as your doctor has told you. Your doctor will decide your daily dose. You should check with your doctor or pharmacist if you are not sure.

Depakote treatment must be started and supervised by a doctor specialised in the treatment of bipolar disorders.

How to take your medicine

- Take this medicine by mouth.
- Swallow the tablets whole with a drink of water. **Do not** crush or chew them.
- This medicine can be taken with or after a meal.
- 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 much to take

Adults (including the elderly)

- **Starting dose is 750mg on the first day. This is usually taken as 2 or 3 divided doses.**
- **The usual dose is then increased to 1000-2000mg each day.**
- Your doctor may decide to increase your dose depending on your illness.

If you have kidney problems

- Your doctor may decide to lower your dose.

Children and adolescents under 18 years of age

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

Tests

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

If you take more Depakote than you should

If you or someone else has taken more Depakote than you should, talk to a doctor or go to your nearest hospital casualty department straight away. Remember to take the medicine pack with you. This is so the doctor knows what you have taken.

The following effects may happen: being sick, headache, blurred eyesight due to pupils of the eyes becoming smaller, lack of reflexes, confusion 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 Depakote

If you forget to take a dose at the right time, take it as soon as you remember. **Do not** take a double dose to make up for a forgotten dose.

If you stop taking Depakote

Keep taking your medicine until your doctor tells you to stop. Do not stop taking Depakote just because you feel better. If you stop, your illness may return.

When your doctor says that you can stop taking Depakote, your dose will be lowered gradually. Your doctor will help you to do this.



If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

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

Allergic reactions

If you have an allergic reaction, stop taking Depakote and see a doctor or go to a hospital straight away. The signs may include: 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.

Stop taking Depakote and see your doctor or go to a hospital straight away if you notice a combination of any of the following serious side effects:

The following side effects may be signs of problems with your liver or pancreas and may show as a sudden illness:

- Feeling weak, general feeling of being unwell
- Loss of or decreased appetite (anorexia)
- Feeling drowsy, confused or tired
- Swelling of the feet and legs (oedema)
- Nausea (feeling sick)
- Vomiting (being sick)
- Stomach pain. Sometimes may be severe and reach through to your back
- Recurrence of fits (seizures) for patients with epilepsy
- Yellowing of the eyes or skin

The following side effects may be signs of problems with your blood cells:

- Bruising more easily, spontaneous bruising or bleeding
- Frequent infections such as fever, severe chills, sore throat or mouth ulcers
- Getting more infections than usual
- Feeling weak, tired, faint, dizzy or having an unusually pale skin

These could be caused by a blood disorder called 'thrombocytopenia'. It can 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.

Other serious side effects which need urgent medical attention:

- Fits (seizures), loss or reduction of consciousness, seeing or hearing things that are not there (hallucinations)
- Memory problems, reduced ability to perform mental tasks, being unable to concentrate
- Difficulty in speaking or slurred speech
- Muscle weakness, lack of co-ordination, muscle twitching or sudden jerks and shaking
- Difficulty in walking or unusual involuntary movements, such as unusual eye movements
- Blistering, peeling, bleeding, scaling or fluid filled patches on any part of your skin. This includes your lips, eyes, mouth, nose, genitals, hands or feet. You may also have flu-like symptoms and fever, joint aches and pains, swollen joints, headaches, chest pain and shortness of breath
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism)
- Breathing difficulty and pain due to inflammation of the lungs (pleural effusion)
- Rapid, uncontrollable movement of the eyes
- An increase in the number and severity of convulsions in patients with epilepsy

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

- Unusual behaviour including being very alert, and sometimes also aggressive, hyperactive and showing bad behaviour
- Water retention which may cause swollen arms or legs
- Bleeding a lot from a wound

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days:

- Swelling of gums or sore mouth
- Nail and nail bed disorders
- Increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest, acne or thinning hair.
- Hair disorders (changes in texture, colour or growth), temporary hair loss
- Diarrhoea
- Night sweats or joint pain
- Irregular periods or a lack/absence of menstrual periods
- Breast enlargement in men
- Loss of hearing
- Double vision
- Kidney disease, kidney problems, blood in the urine, bedwetting or increased need to pass urine, urinary incontinence (unintentional passing of urine)
- Obesity, weight gain – as your appetite may be increased
- Headache
- Seeing or hearing things that are not there (hallucinations)
- Aggression, agitation, disturbance in attention, abnormal behaviour, restlessness/hyperactivity, and learning disorder
- Tingling or numbness in the hands and feet
- Lowering of normal body temperature
- Abnormal blood clotting factors
- Muscle pain and weakness (rhabdomyolysis)

Bone disorders

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

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

Male fertility

Taking Depakote can be a contributing factor in male infertility.

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 Depakote

Keep this medicine in a safe place where children cannot see or reach it.

Do not use Depakote after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Depakote 250mg Tablets contain

- Each 250mg tablet contains 269.1mg of the active substance, valproate semisodium (equivalent to 250mg of valproic acid).
- The other ingredients are: silicone dioxide, pregelatinised starch, povidone, titanium dioxide (E171), hypromellose, polyethylene glycol 6000, Methacrylic acid-ethyl acrylate copolymer (1:1), triethyl citrate, vanillin, sunset yellow aluminium lake (E110).

What Depakote 500mg Tablets contain

- Each 500mg tablet contains 538.2mg of the active substance, valproate semisodium (equivalent to 500mg of valproic acid).
- The other ingredients are: silicone dioxide, pregelatinised starch, povidone, titanium dioxide (E171), hypromellose, polyethylene glycol 6000, Methacrylic acid-ethyl acrylate copolymer (1:1), triethyl citrate, vanillin, ponceau 4R aluminium lake (E124), indigotine aluminium lake (E132).

What Depakote Tablets look like and contents of the pack

- Depakote 250mg Tablets are oval orange gastro-resistant tablets supplied in Aluminium/aluminium blister packs containing 30, 60 or 90 tablets.
 - Depakote 500mg Tablets are oval lilac pink gastro-resistant tablets supplied in Aluminium/aluminium blister packs containing 30, 60 or 90 tablets.
- Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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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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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