

Package leaflet: Information for the user

[QR code to be included:]

<https://www.medicines.org.uk/emc/product/293/rmms>

▼ 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.

Episenta solution for injection (Sodium Valproate 100 mg/ml)

WARNING

Episenta Injection, sodium valproate 100 mg/ml, 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 Episenta Injection. 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 Episenta Injection unless your doctor tells you to as your condition may become worse.

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

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

1. What Episenta Injection is and what it is used for

Episenta Injection contains sodium valproate, which belongs to a group of medicines called antiepileptics. These are used to control epileptic seizures.

Episenta solution for injection is used to treat various types of epileptic seizures (fits) when it is not possible to take sodium valproate tablets.

2. What you need to know before you take Episenta Injection

Do not use Episenta Injection

- if you are allergic to sodium valproate or any of the other ingredients of this medicine (listed in section 6).
- if you, or a member of your family, have or have had severe liver problems.
- if you suffer from a disease called porphyria (a rare condition that affects the breakdown of components of red blood cells).
- if you have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome).
- if you suffer from urea cycle disorder (a certain metabolic disorder).
- You must not use Episenta Injection if you are pregnant, unless nothing else works for you.
- if you are a woman able to have a baby, you must not take Episenta Injection unless you use effective method of birth control (contraception) during your entire treatment with Episenta Injection. Do not stop taking Episenta Injection 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 Episenta Injection.

Warnings and precautions

A small number of people being treated with antiepileptics 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 antiepileptic 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 Episenta Injection if:

- you have 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 give you a lower dose.
- you have a 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 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 Episenta Injection.

Weight gain

Having Episenta Injection 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 having Episenta Injection and during your treatment.

Other medicines and Episenta Injection

Tell your doctor, pharmacist or nurse 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 Episenta Injection can affect the way some other medicines work. Also some medicines can affect the way Episenta Injection works.

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

- 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, rufinamide, topiramate, lamotrigine and felbamate.
- acetazolamide used to treat glaucoma, edema or fits

Episenta Injection may increase the effect of the following medicines:

- medicines used for thinning the blood (such as warfarin)
- zidovudine used to treat HIV infection
- temozolomide used to treat cancer
- medicines for depression
- monoamine oxidase inhibitors (MAOI) such as moclobemide, selegiline, linezolid
- medicines used to calm emotional and mental health problems (including schizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine
- nimodipine
- propofol – used for anaesthesia

The following medicines can affect the way Episenta Injection works:

- oestrogen-containing products (including some birth control pills)
- some medicines used for the prevention and treatment of malaria such as mefloquine and chloroquine
- cimetidine used for stomach ulcers
- protease inhibitors such as lopinavir and ritonavir – used for HIV infection and AIDS
- antibiotics e.g. erythromycin, 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.
- rifampicin used to treat tuberculosis and other infections
- cholestyramine used to lower blood fat (cholesterol) levels
- metamizole, a medicine used to treat pain and fever

It may still be possible for you to be given Episenta Injection; your doctor will advise you on what is suitable for you.

Taking Episenta Injection with food and drink

Alcohol intake is not recommended during treatment.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Important advice for women

- For epilepsy, you must not use Episenta Injection 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 Episenta Injection unless you use effective method of birth control (contraception) during your entire treatment with Episenta

Injection. Do not stop taking Episenta Injection 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. 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.
- 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 to 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 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 baby 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 their first period (menarche).
- 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 EPISENTA INJECTION
- ☐ I AM TAKING EPISENTA INJECTION AND NOT PLANNING TO HAVE A BABY
- ☐ I AM TAKING EPISENTA INJECTION AND PLANNING TO HAVE A BABY
- ☐ I AM PREGNANT AND I AM TAKING EPISENTA INJECTION

I AM STARTING TREATMENT WITH EPISENTA INJECTION

If this is the first time you have been prescribed Episenta Injection 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 Episenta Injection. 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 Episenta Injection 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 Episenta Injection.
- 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.
- 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 EPISENTA INJECTION AND NOT PLANNING TO HAVE A BABY

If you are continuing treatment with Episenta Injection but you are not planning to have a baby make sure you are using an effective method of contraception without interruption during your entire treatment with Episenta Injection. 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 Episenta Injection.
- 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.
- 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.
- 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 EPISENTA INJECTION 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 Episenta Injection 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 Episenta Injection or switch you to another medicine, or stop treatment with Episenta Injection, 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 Episenta Injection 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 Episenta Injection 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 EPISENTA INJECTION

Do not stop taking Episenta Injection, 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 Episenta Injection 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 Episenta Injection 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 Episenta Injection 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

A small amount of sodium valproate, the active substance of Episenta Injection, gets into the breast milk. Talk to your doctor about whether you should breast-feed your baby.

Fertility

Episenta Injection may decrease your fertility. However, single reports have shown that this effect is reversible after discontinuation of the medicine.

Driving and using machines

You may experience drowsiness when you are first given Episenta Injection, or if you are also taking other medicines, such as other antiepileptic drugs or benzodiazepines. If affected, you should not drive or operate machinery.

Episenta Injection contains sodium

This medicine contains 41.6 mg sodium (cooking/table salt) in each 3 ml ampoule. This is equivalent to 2 % of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 138.8 mg sodium (cooking/table salt) in each 10 ml ampoule. This is equivalent to 7 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Episenta Injection

Episenta Injection treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

Dosage

Your doctor will decide on the amount of Episenta Injection you will be given. This will depend on your age and weight and will be adjusted to achieve adequate control of your seizures. If you have been taking sodium valproate by mouth, the dose given to you will be the same by injection. If you have been receiving other medicines for epilepsy the dose of Episenta Injection will be increased gradually over about 2 weeks. The total daily dose will normally be given by three or four slow injections, lasting 3-5 minutes, into your veins during the day, or by a continuous infusion (drip).

Adults, including the elderly

The recommended starting dose is 400–800 mg (4–8 ml) daily increasing by 150–300 mg (1.5–3.0 ml) every 3 days, until the seizures are controlled. The maximum daily dose you should receive is 2,500 mg (25 ml).

Your doctor may decrease your dose if you are taking other antiepileptic drugs, have poor kidney function or you are an elderly patient.

Children and adolescents

The dose for children will depend on their weight. This is usually 20–40 mg (0.2–0.4 ml) for each kg of body weight.

Your treatment with Episenta Injection will be changed to oral therapy (by mouth) as soon as possible.

Patients with kidney problems

Your doctor may decide to adjust your dose.

Patients taking other medicines for fits (epilepsy)

You or your child may be taking other medicines for epilepsy at the same time as Episenta Injection. If so, your doctor should gradually initiate treatment depending on your or your child's condition.

Your doctor may increase the dose of Episenta Injection by 5–10 mg for each kg of body weight each day depending on which other medicines you are taking.

If you think you have missed a dose or been given more Episenta Injection than you should

Episenta Injection will be given to you by a doctor, who will ensure that the correct dose is given for your condition. If you have any concerns tell your doctor or nurse.

If you stop using Episenta Injection

It is important for you to keep having your Episenta Injection treatment until your doctor decides to stop. If you stop, your seizures may return.

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. Episenta Injection 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 Episenta Injection.

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

4. Possible side effects

Like all medicines this medicine 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 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 (also known as DRESS syndrome).
- Liver problems and problems of the pancreas may show as a sudden illness which may happen in the first six months of treatment. 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. It may sometimes even lead to death. Your doctor may tell you to stop taking Episenta Injection immediately if you have these symptoms.
- 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'.
- 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, 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, hyperactive and unusual or inappropriate behaviour. This is more likely if other medicines to treat fits such as phenobarbital and topiramate are taken at the same time or if the Episenta Injection 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.
- An increase in the number and severity of convulsions.

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), stomach ache or diarrhoea, especially when starting treatment.
- Swelling of gums or sore mouth
- Feeling dizzy
- Fainting
- Hearing loss
- Double vision
- Nail and nail bed disorders
- Skin problems such as rashes. These happen rarely, but more often in people also taking lamotrigine.
- Hair disorders (changes in texture, colour or growth), hair loss which is usually temporary. When it grows back it may be more curly than before.
- Increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest, acne or thinning hair.
- Skin rash caused by narrow or blocked blood vessels (vasculitis)
- Changes in women's periods and increased hair growth in women
- Breast enlargement in men
- Swelling of the feet and legs (oedema)
- Obesity, weight gain – as your appetite may be increased
- Kidney disease, kidney problems, blood in the urine, bedwetting or increased need to pass urine, unintentional passing of urine (urinary incontinence)
- 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 antiepileptic medication, have a history of osteoporosis, or take steroids.

Tests

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

Male fertility

Taking Episenta Injection can be a contributing factor in male infertility.

If you, or your carer, notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

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 behavior, 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 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 Episenta Injection

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

Do not use this medicine after the expiry date which is stated on the label after “Exp.:”. The expiry date refers to the last day of that month.

Do not use this medicine if you notice signs of deterioration such as crystallisation or discolouring.

Do not freeze the medicine.

Episenta solution for injection may be diluted with 0.9 % saline or 5 % dextrose before infusion. Your hospital pharmacy will ensure that the solution for injection is diluted and stored in an appropriate manner.

6. Contents of the pack and other information

What Episenta Injection contains:

- The active substance is sodium valproate 100 mg per ml.
- The other ingredients are disodium edentate and water for injections.

What Episenta Injection looks like and contents of the pack

Episenta solution for injection is a clear colourless solution. It is available in glass (type I) ampoules with silicone coating on the inside containing either 3 ml or 10 ml of the solution for injection. Each pack contains 5 ampoules.

Marketing Authorisation Holder and Manufacturer

Desitin Arzneimittel GmbH
Weg beim Jäger 214
D-22335 Hamburg, Germany
e-mail: medinfo@desitin.co.uk

This leaflet was last revised in 12/2021.