Package leaflet: Information for the patient

Pro-Epanutin® 75 mg/mL concentrate for solution for infusion/solution for injection
fosphenytoin sodium

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 or nurse.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- You may have been given Pro-Epanutin as a single dose to control status epilepticus. In this case, you will only be able to read this leaflet after you have had the product given to you. Your doctor will have considered the important safety information in this leaflet, but your urgent need for treatment may have been more important than some of the normal cautions. Check them now, especially if you are going to continue to be given Pro-Epanutin (or any other form of phenytoin).

What is in this leaflet

1. What Pro-Epanutin is and what it is used for

Pro-Epanutin contains the active substance fosphenytoin which belongs to a group of medicines called anti-epileptic medicines; these medicines are used to treat epilepsy.

Pro-Epanutin is used in adults and children aged 5 years and older:

- to treat severe epileptic seizure or fits (status epilepticus) of the tonic-clonic (grand mal) type.
- to control or prevent seizures during or after brain surgery and/or head injury.
- to control or prevent seizures for short periods of time when anti-epileptic medicines cannot be taken by mouth.

You should consult your doctor if you are unsure why you have been given Pro-Epanutin.

2. What you need to know before you are given Pro-Epanutin

You must not be given Pro-Epanutin

– if you are allergic to fosphenytoin sodium, phenytoin or any of the other ingredients of this medicine (listed in section 6).
– if you have problems with your heart rhythm.
– if you have acute intermittent porphyria (suffer from a genetic disorder affecting the formation of red blood cells).
– if you are taking delavirdine, an antiviral medicine used to treat human immunodeficiency virus (HIV) infection.

Please tell your doctor if you have had any of these conditions. If you have any questions, ask your doctor or pharmacist or nurse.

Warnings and precautions

Talk to your doctor or pharmacist or nurse before taking Pro-Epanutin if you have had any of the following conditions:

- Liver disease.
- Heart disease or stroke.
- Low blood pressure or heart failure.
- Kidney disease.
- Low protein (albumin) in your blood.
- Diabetes.
- Special diet which restricts your phosphate intake.

Reduced blood pressure and serious heart problems may occur during the use of Pro-Epanutin. These side effects may be worse in elderly patients, children, or patients who are very ill. Your doctor will therefore monitor your heart, blood pressure and breathing function when you are given Pro-Epanutin for the duration of the infusion and for approximately 30 minutes after the end of the infusion.

A small number of people being treated with anti-epileptics such as fosphenytoin have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

In the general population, serious skin side effects can rarely occur during treatment with Pro-Epanutin; for signs and symptoms of serious skin reactions and what action to take please see section 4. In people of Chinese or Asian origin this risk may be associated with a variant in genes. If you are of Chinese or Asian origin and tests have shown that you carry the genetic variant HLA-B*1502, or if you are of Taiwanese, Japanese, Malaysian or Thai origin and tests have shown that you carry the genetic variant CYP2C9*3, discuss this with your doctor before taking Pro-Epanutin.

Cases of swelling of the face, mouth (lip, gum, tongue) and throat that can lead to life-threatening breathing difficulty have been reported in people being treated with phenytoin and fosphenytoin. If at any time you have these signs or symptoms immediately contact your doctor.

There is a risk of harm to the unborn child if Pro-Epanutin is used during pregnancy. Women of childbearing age should use effective contraception with Pro-Epanutin (see ‘Pregnancy and breast-feeding’ and ‘Contraception in women’).

Other medicines and Pro-Epanutin

Tell your doctor or pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

Some medicines can affect the way Pro-Epanutin works, or Pro-Epanutin itself can reduce the effectiveness of other medicines taken at the same time. It is important that your doctor get knowledge of **all** other medicines you take. This includes medicines available with and without prescription (including folic acid and vitamin D) and herbal medicines.

The list below only includes the conditions being treated and not the actual active substances. Your doctor or pharmacist will be able to give you more information.

Talk to your doctor or pharmacist if you take any medicines to treat, prevent or used for:

- heart and circulation problems
- blood clotting disorders
- epilepsy
- fungal infections
- human immunodeficiency virus (HIV) infection
- tuberculosis and other infections
- stomach ulcers or heart burn
- asthma and bronchitis (theophylline)
- pain and inflammation
- sleeplessness, depression and psychiatric disorders
- diabetes
- cancer
- rejection in case of organ and tissue transplants or if you take corticosteroids
- hormone replacement therapies (oestrogens), oral contraceptives (the birth control pill) (see 'Pregnancy and breast-feeding' and 'Contraception in women')
- muscle relaxants used for surgery and some anaesthetic medicines

Your doctor may need to test the amount of phenytoin in your blood to help decide if your other medicines are affecting your treatment.

The herbal preparation St John's wort *(Hypericum perforatum)* should not be taken at the same time as this medicine. If you already take St John's wort, consult your doctor before stopping the St John's wort preparation.

Pro-Epanutin may also interfere with certain laboratory tests that could be performed.

Pro-Epanutin with alcohol

Drinking a lot of alcohol or drinking frequently can also affect the concentration of Pro-Epanutin in your blood.

Pregnancy and breast-feeding

<u>Pregnancy</u>

If you are pregnant or think you may be pregnant, consult your doctor promptly. You should not stop taking your medicine until you have discussed this with your doctor. Stopping your medication without consulting your doctor could cause seizures which could be dangerous to you and the pregnancy. Your doctor may decide to change your treatment. Closer monitoring of your unborn child could also be considered.

Pro-Epanutin may cause birth defects. If you take Pro-Epanutin during pregnancy your baby has a higher risk of having a birth defect. Birth defects which have been reported include facial, skull, nail, finger and heart abnormalities. Tumors, including nerve cell tumors have been reported in children whose mothers received this medicine during pregnancy.

If you are of childbearing age and plan to become pregnant, consult your doctor for a preconceptional visit. You should discuss your treatment options with your doctor.

If you take Pro-Epanutin during pregnancy, your baby is also at risk for bleeding problems right after birth. Your doctor may give you and your baby a medicine to prevent this. Moreover, your child should be closely monitored.

Breast-feeding
Pro-Epanutin passes into breast milk. You should not take Pro-Epanutin if you are breast-feeding. Ask your doctor for advice.

Contraception in women

If you are of childbearing age, you should discuss your treatment options and effective methods of birth control with your doctor. Pro-Epanutin may result in a failure of hormonal contraceptives, hence you should be counselled regarding the use of other effective contraceptive methods.

Driving and using machines

Pro-Epanutin may cause dizziness or drowsiness. If you experience these symptoms, do not drive or use any tools or machinery.

Pro-Epanutin contains sodium

When calculating the total amount of sodium, any dilution of fosphenytoin sodium injection with sodium chloride solution should be taken into consideration.

Each 10 mL vial contains 85 mg sodium (main component of cooking/table salt). This is equivalent to 4.25% of the recommended maximum daily dietary intake of sodium for an adult.

Each 2 mL vial contains 17 mg sodium, which is less than 1 mmol sodium (23 mg).

3. How Pro-Epanutin is given

You will be in hospital when you are given Pro-Epanutin.

It will be either injected into one of your large veins (intravenous infusion) or into your muscle (intramuscularly). When given intravenously, Pro-Epanutin must be diluted.

You will be monitored continuously by electrocardiogram, blood pressure and respiratory function for the duration of the infusion and for approximately 30 minutes after the end of the infusion.

The dose and concentration of the solution of Pro-Epanutin you are given will be decided by your doctor and will be written as the equivalent dose of phenytoin sodium (PE). The dose will be as milligram per dose if given as an injection or milligram per millilitre (mg/mL) of solution if given as an infusion.

Adults

Severe epileptic seizure or fits (Status epilepticus)

Pro-Epanutin is usually given after treatment with either diazepam or lorazepam injection.

The first dose of Pro-Epanutin is called a loading dose and is injected into your vein. After the loading dose you may receive lower doses of Pro-Epanutin, intravenously or intramuscularly, these are called maintenance doses.

If Pro-Epanutin does not stop your seizures, other treatments will be tried.

Brain surgery or head trauma

The first dose is called a loading dose and is injected into your vein or into your muscle. After the loading dose you may receive lower doses of Pro-Epanutin, intravenously or intramuscularly, these are called maintenance doses.

Maintenance doses

Your doctor may take samples of your blood to help decide the right maintenance dose for you.

If your doctor decides that you need to continue treatment, you will be transferred to treatment by mouth when appropriate. This will be with phenytoin because Pro-Epanutin (fosphenytoin) cannot be taken by mouth.

Temporary replacement of oral phenytoin treatment

If you are given Pro-Epanutin because you cannot take phenytoin by mouth, you will not need a loading dose and the dose you are given will be the same as your dose of phenytoin. Because the dose of Pro-Epanutin is given in PE (phenytoin sodium equivalents), the number of mg PE of Pro-Epanutin you are given should be the same as the number of mg of phenytoin sodium you take by mouth.

Children aged 5 years and older

The doses of Pro-Epanutin per kilogram of body weight are the same for children (aged 5 years and older) as for adults.

Pro-Epanutin is given to children aged 5 years and older by a drip (infusion) into the vein (intravenous) only.

Elderly patients over 65 years, the very ill and patients with kidney or liver disease

The dose of Pro-Epanutin may be reduced or the injection given into the vein at a slower rate.

If you are given more Pro-Epanutin than you should

Pro-Epanutin is dangerous in overdose. However, Pro-Epanutin is given to you in a hospital and the dose is calculated for you individually and the doctor will monitor you during treatment and cardiac resuscitative equipment will be available. If you think you have been given too much Pro-Epanutin, contact your doctor immediately.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor **immediately** if you experience any of the following symptoms after taking this medicine. Although they may be rare, these symptoms can be serious.

– Uncommon: may affect up to 1 in 100 people

- If you develop a **severe skin rash that causes blistering**, (this can also affect the mouth and tongue), these skin reactions are often accompanied by **fever or flu-like symptoms**. These may be signs of a condition known as Stevens Johnson Syndrome, or toxic epidermal necrolysis (TEN). Your doctor will stop your treatment in these cases.

– Not known: frequency cannot be estimated from the available data

- If you notice **bruising, fever, you are looking pale or a severe sore throat**. These may be the first signs of an abnormality of the blood, such as decreases in the number of red cells, white cells or platelets. Your doctor may take regular blood samples to test for these effects.
- **Skin rash and fever with swollen glands, yellow skin and eyes**, particularly in the first two months of treatment, as these may be signs of a hypersensitivity reaction. If these are severe and you also experience pain and inflammation of the joints this could be related to a condition called systemic lupus erythematosus.
- If you experience **skin discolouration, swelling and pain** where the injection was given which then starts to spread down your arm to your hands and fingers. This may mean you have a condition known as “purple glove syndrome”. In most cases this will improve on its own but in some cases it can be serious and require urgent medical treatment.
- Areas of red skin with small elevated **sterile pustules (small blisters filled with white/yellow fluid)**. There tends to be more disease in skin folds. Swelling of the face can occur as well (Acute Generalised Exanthematous Pustulosis [AGEP]).
- **Skin rash, fever, swollen glands, increase in a type of white blood cell (eosinophilia), and inflammation of internal organs** (liver, lungs, heart, kidneys and large intestine), as they may be signs of a hypersensitivity reaction (Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]).

- If you experience a state of **confusion or severe mental illness**, as this may be a sign that you have high amounts of phenytoin in your blood. On rare occasions, when the amount of phenytoin in the blood remains high, irreversible brain injury has occurred. Your doctor may test your blood to see how much phenytoin is in the blood and may change your dose.
- **Sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching** (especially affecting the whole body) as this may be a sign of a hypersensitivity reaction.

Other side effects that may occur are:

– Very common: may affect more than 1 in 10 people
- unusual eye movements, dizziness.
- itching.

– Common: may affect up to 1 in 10 people
- mood swings, pins and needles, unsteadiness, drowsiness, headaches, shaking, abnormal or uncoordinated movements, slurred speech, blurred vision, taste disturbance.
- ringing in the ears, vertigo.
- feeling sick, dry mouth, being sick.
- pain or reaction at the site of injection.
- loss of energy or strength, chills.
- decreased level of consciousness.
- visual disturbances.
- reduced blood pressure.
- bruising.

– Uncommon: may affect up to 1 in 100 people
- nervousness, confusion, abnormal/irrational thoughts.
- numbness or tingling in the extremities.
- increased or decreased reflexes.
- double vision, loss of hearing.
- loss of sensation in the tongue.
- skin rash including measles-like reactions which are mild.
- muscle weakness, twitching muscles, muscle spasms.

– Not known: frequency cannot be estimated from the available data
- swelling of the lymph glands.
- inflammation of the wall of the arteries, problems with the body's defence against infection.
- increased levels of blood sugar, or decreased levels of blood calcium, folic acid and vitamin D. If you also do not get enough vitamin D in your diet or from exposure to sunlight, you may suffer from bone pain or fractures.
- 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 medicines, have a history of osteoporosis, or take steroids.
- change in appetite, difficulty in controlling movements, sleeplessness, convulsions.
- inflammation of the lining of the lung, problems breathing.

- enlarged gums, constipation.
- inflammation of the liver, liver damage (seen as yellowing of the skin and whites of the eye).
- increased or abnormal body or facial hair, changes in facial features, enlarged lips, changes in the hands with difficulty in straightening the fingers.
- inflammation of the kidneys.
- temporary itching, burning, warmth or tingling in the groin may sometimes occur during or shortly after injection of Pro-Epanutin into your vein. Your doctor may reduce the rate at which Pro-Epanutin is injected or temporarily stop injecting Pro-Epanutin if you feel these sensations.
- hives.
- abnormal levels of proteins in the blood that help the body defend against germs.
- serious heart problems.
- painful, curved penile erections.

Reporting of side effects
If you get any side effects, talk to your doctor or 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 Pro-Epanutin

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 carton and vial after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C). The undiluted product may be stored at room temperature (8 °C to 25 °C) for up to 24 hours.

After dilution, this medicine is suitable only for immediate use. For single use only. After opening, unused product should be discarded.

Vials that develop particulate matter should not be used.

6. Contents of the pack and other information

What Pro-Epanutin contains

– The active substance is fosphenytoin sodium. Each mL contains 75 mg fosphenytoin sodium. This is equivalent to 50 mg phenytoin sodium (referred to as 50 mg PE).

Each vial of 2 mL contains 150 mg of fosphenytoin sodium (equivalent to 100 mg phenytoin sodium and referred to as 100 mg PE).

Each vial of 10 mL contains 750 mg of fosphenytoin sodium (equivalent to 500 mg phenytoin sodium and referred to as 500 mg PE).

– The other ingredients are water for injection, trometamol and hydrochloric acid.

What Pro-Epanutin looks like and contents of the pack

Pro-Epanutin concentrate for solution for infusion/solution for injection comes in glass vials containing 10 mL or 2 mL of a clear, colourless to pale yellow, sterile solution.

Pro-Epanutin is available in packs containing 5, 10 or 25 vials of 2 mL solution. Pro-Epanutin is also available in multipacks comprising of 10 boxes each containing 5 vials with 2 mL solution (= 50 vials).

Pro-Epanutin is available in packs containing 5 or 10 vials of 10 mL solution. Pro-Epanutin is also available in multipacks comprising of 5 boxes each containing 5 vials with 10 mL solution (= 25 vials).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ

Manufacturer

Pfizer Service Company BV
Hoge Wei 10
1930 Zaventem
Belgium

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

France - Prodilantin
Denmark, Finland, Ireland, Sweden, United Kingdom (Northern Ireland) - Pro-Epanutin

This leaflet was last revised in 11/2024.

Other sources of information

Detailed information on this medicine is available on the web site of: MHRA

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