UNIVAL SYRUP 200MG/5ML
UNIVAL ENTERIC COATED TABLET 200MG

Sodium Valproate

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What UNIVAL is used for

Generalized Seizures:

Petit mal which includes:

- Absence.
- Myoclonic-astatic (Lennox).
- Blitz-Nick-Salaam (BNS) syndrome.

Grand mal.

Grand mal and petit mal.

Partial (focal) seizures:

Motor (Jackson, adversions).

Psychomotor.

How UNIVAL works

Sodium Valproate is an anti-epileptic and anticonvulsive agent. By inhibiting aminobutyrate aminotransferase activity, Valproate increases the level of y-aminobutyric acid (GABA) in the CNS. GABA inhibits pre- and post-synaptic discharges. Valproate contains no nitrogen atom thus differing completely from the structure of the commonly used anticonvulsive agents.

Before you use UNIVAL

WARNINGS FOR WOMEN AND GIRLS

Before you start to use it:

This medicine can seriously harm an unborn baby.

Always use effective contraception during treatment with sodium valproate.

If you are thinking about becoming pregnant, or if you are pregnant, contact your doctor urgently.

You must CONTINUE taking sodium valproate unless your doctor tells you to stop.

- *When you must not use it*

Do not take sodium valproate if:

- You are allergic (hypersensitive) to sodium valproate or any of the other ingredients of UNIVAL.
- You have liver problems or you or your family have a history of liver problems.
- You have a rare illness known as porphyria (a type of blood disorders).
- You are pregnant, unless nothing else works for you.

Do not use this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist.

- *Before you start to use it*

A small number of people being treated with sodium valproate have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

Check with your doctor before taking this medicine if:

- You have diabetes. This medicine may affect the result of urine tests.
- 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 erythematous (SLE) – a disease of the immune system which affects skin, bones, joints and internal organs.
- You are pregnant or you are a woman of child-bearing age.
- If you are a woman able to have a baby, you must not take sodium valproate unless you use an effective method of birth control (contraception) at all times during your treatment with sodium valproate.
- You have mitochondrial disorders caused by mutations in thenuclear gene encoding mitochondrial enzymepolymerase γ (POLG, e.g. Alpers- Huttenlocher Syndrome) and in children under two years of age who are suspected of having a POLG-related disorder.

Taking sodium valproate with drink

Alcohol intake is not recommended during treatment.

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Weight gain:
Taking sodium valproate may make you put on weight.

Blood test:
Your doctor may wish to do blood tests before you start taking sodium valproate and during your treatment.

- *Taking other medicines*

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

- Some medicines used for pain and inflammation such as aspirin.
- Some other medicines used to treat fits (epilepsy) such as *phenobarbital, primidone, phenytoin, carbamazepine, rufinamide, topiramate, acetazolamide, lamotrigine* and *felbamate.*

Sodium valproate 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
- Nimodipine
- Medicines used to calm emotional and mental health problems (including schizophrenia, bipolar disorder and depression) such as quetiapine, diazepam and olanzapine.

The following medicines can affect the way sodium valproate works:

- Oestrogen-containing products (including some birth control pills).
- Some medicines used for the prevention and treatment of malaria such as mefloquine and chloroquine.
- Protease inhibitors such as lopinavir and ritonavir – used for HIV infection and AIDS.
- Cimetidine used for stomach ulcers.
- Some medicines used for infections (antibiotics) such as rifampicin dan erythromycin.
- Carbapenem agents (antibiotics used to treat bacterial infections) such as imipenem, meropenem and panipenem. The combination of sodium valproate and Carbapenem agents should be avoided because it may decrease the effect of your medicine.
- Cholestyramine used to lower blood fat (cholesterol) levels.

Some medicines and sodium valproate may interfere with each other, these include propofol (a medicine used before and during general anaesthesia).

Tell your doctor that you are taking UNIVAL if you are going for an operation.

How to use UNIVAL

Always take sodium valproate as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

- Your doctor will decide the dose to give you or your child depending on you or your child's body weight.
- Take this medicine by mouth.
- Do not chew or crush the tablets.

- *How much to use*

- *Adults (including the elderly)*

The starting dose is 600mg daily with gradually increment by 200mg every 3 days depending on your condition.
The usual dose is between 1000mg and 2000mg daily. This may be increased to 2500mg.

- *Children over 20 kilograms*

The starting dose should be 400mg daily (irrespective of weight). This may be further increased to 35mg for each kilogram of body weight each day depending on your child's condition.

- *Children under 20 kilograms*

It is recommended to use sodium valproate syrup.
The usual dose is 20mg for each kilogram of body weight each day. Depending on the child's condition, doctor may decide to increase this dose which above 40mg for each kilogram each day (40mg/kg/day) and require monitoring.

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• *If you have kidney problems*
Your doctor may decide to adjust you or your child's dose.

• *Patients taking other medicines for 'fits' (epilepsy)*
Your doctor may increase the dose of sodium valproate by 5 to 10mg for each kilogram of body weight each day depending on which other medicines you are taking.

- *When to use it*
Sodium valproate should be administered with or after meals. Take sodium valproate at about the same time each day unless you doctor tells you otherwise.

- *How long to use it*
Sodium valproate must be taken regularly for as long as your doctor prescribed it. Do not discontinue treatment unless advised to do so by your doctor.

- *If you forget to use it*
If you missed 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 use too much (overdose)*
If you take sodium valproate more than you should, tell a doctor or go to hospital emergency department straight away. Take the medicine pack with you. The following effects may happen: feeling sick or being sick, the pupils of the eyes get smaller, dizziness, weak muscles, poor reflexes, breathing problems and fits (seizure).

While you are using it
- *Things you must do*
• Schedule an urgent appointment with your doctor if you want to become pregnant or if you think you are pregnant. Tell your doctor immediately if you are pregnant or breast-feeding.
You should not take sodium valproate if you are pregnant or a woman of child-bearing ageunless explicitly advised by your doctor.
• If you are a parent or a caregiver of a female child treated with sodium valproate, you should contact their doctor once your child experiences their first period (menarche).

Breast-feeding
Very little sodium valproate gets into the breast milk. Talk to your doctor before breastfeeding your baby.

- *Thing you must not do*
• Do not give this medicine to anyone else, even if they have the same condition as you.
• Do not use this medicine to treat any other complaints unless your doctor tells you to.
• Do not stop taking sodium valproate, or change the dosage without checking with your doctor.
• Continue taking sodium valproate or using your birth control (contraception) until you have discussed your pregnancy or your plan to get pregnant with your doctor.

- *Things to be careful of*
• Driving and using machines:
You may feel sleepy when taking sodium valproate. If this happens to you, do not drive or use any tools or machines. Taking other antiepileptic medicines may increase sleepiness.
• In patients with diabetes mellitus, the content of sucrose in Sodium Valproate Syrup should be taken into consideration.
• Sodium valproate can seriously harm an unborn baby when taken during pregnancy.
• The higher the dose, the higherthe risks but all doses carry a risk.
• It can cause serious birth defects and can affect the way in which the child develops as it grows. Birth defects which have been reported include *spina bifida* (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects.
• If you take sodium 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 it is known 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 do not have epilepsy.
• It is estimated that up to 30-40% of preschool children whose

mothers took valproate during pregnancy may have problems with early childhood development. Children affected can be slow to walk and talk, intellectually less able than other children, and have difficulty with language and memory.

- Autistic spectrum disorders are more often diagnosed in children exposed to valproate and there is some evidence children may be more likely to develop symptoms of Attention Deficit Hyperactivity Disorder (ADHD).

Important advice for male patients able to father a child

Potential risk related to taking valproate in the 3 months prior to conception.

A study suggests that if you take valproate in the 3 months prior to conception, your child may have a higher risk for impaired mental and/or motor development compared to children born to fathers who used lamotrigine or levetiracetam, other medicines that can be used to treat your disease. In this study, around 5 children in 100 had such disorders when born from fathers treated with valproate, and around 3 children in 100 when born from fathers treated with the other medicines. There are no data on this potential risk to children fathered more than 3 months after stopping valproate treatment (the time needed for new sperm to be formed).

As a precautionary measure, your doctor will discuss with you

- The potential risk when fathering a child if you are treated with valproate,
- The need to use effective contraception (birth control) for you and your female partner during the treatment and for 3 months after stopping valproate
- The need to consult your doctor to discuss alternative treatment options, as soon as you are planning to father a child and before discontinuing contraception (birth control),
- To not donate sperm during treatment and for 3 months after stopping
  treatment.

Do not stop your treatment without talking to your doctor. If you stop your treatment, your symptoms may become worse. If your female partner becomes pregnant while you used valproate in the 3 months prior to conception, both of you should contact the doctor for counselling.

You should get regular (at least annual) appointments with your doctor. During this visit your doctor will make sure you acknowledge the risk and precautions associated with valproate use. Make sure you read the patient guide that you will receive from your doctor.

Side effects

Tell your doctor straight away ifyou notice any of the following serious side effects which may need urgent medical treatment:

- Rashes, swallowing or breathing problems, swelling of your lips, face, throat or tongue. Hands, feet or genitals may also be affected.
- Liver injury and increased liver enzyme.

Your doctor may tell you to stop taking sodium valproate immediately if you have these symptoms:

- Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme.
- Osteopenia and osteoporosis (thinning of the bone) and fractures.
- A decrease in the number of blood platelets and red blood cells.
- Blood clotting problems, bruising or bleeding for no reason.
- Changes in mood, loss of memory, confusion, lack of concentration and deep loss of consciousness (coma).
- Underactive thyroid gland, which may cause tiredness or weight gain (hypothyroidism).
- Breathing difficulty and pain due to inflammation of the lungs (pleural effusion).

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

- Changes in behavior including being very alert, and sometimes also aggressive, hyper-active and unusual or inappropriate behavior.
- 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.
- Rapid, uncontrollable movement of the eyes.

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days:
- Feeling sick, being sick (vomiting), stomach ache or diarrhea, especially when starting treatment. This may be helped by taking the tablets with food.
- Swelling of gums or sore mouth
- Involuntary muscle movement
- Fainting
- Double vision (diplopia)
- Nail and nail bed disorders
- Hearing loss
- Rashes
- Acne
- Hair disorders (changes in texture, color or growth), hair loss which is usually temporary. When it grows back it may be curlier 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 problems, blood in the urine, bedwetting or increased need to pass urine, urinary incontinence (unintentionalpassing of urine).
- Headache
- Aggression, agitation, disturbancein 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).
- Male infertility (may be reversible after dose reduction or discontinuation).

You may report any side effects or adverse drug reactions directly toThe National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) orVaccines (AEFI)].

Storage and Disposal of UNIVAL

- *Storage*
- Keep out of reach and sight of children.
- Do not use UNIVAL after the expiry date.
- Store in a dry place below 30°C.

- *Disposal*

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.

Product description

- *What it looks like*
- **UNIVAL 200mg/5ml syrup** is pink, slightly viscous syrup in bottles of 100 ml.
- **UNIVAL 200mg Enteric Coated Tablets** are white to off white rounded biconvex enteric coated tablet in packs of 50 tablets.

Ingredients

- Each 5mL of **UNIVAL 200mg/5ml syrup** contains:

- Active ingredient: Sodium valproate 200mg
- Inactive ingredients: Sucrose, Usacert FD & C red No. 40, Cherry Flavor Liquid & Purified water

- Each **UNIVAL 200mg Enteric Coated Tablet** contains:

- Active ingredient: Sodium valproate 200mg
- Inactive ingredients: Talc, Calcium Silicate, Sodium Starch Glycolate, Aerosil 200 Magnesium Stearate, Opadry Y-1 7000 White & Opadry OY-P 7171white.

- *MAL Numbers:*
- **UNIVAL 200mg/5ml Syrup** MAL07082854AZ
- **UNIVAL 200mg Enteric Coated Tablet** MAL08031348AZ

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UNIVAL ENTERIC COATED TABLET 200MG

Sodium Valproate

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