VALEPTIC CR can seriously harm an unborn child when taken during pregnancy. It can cause serious birth defects to body organs and/or body structures as well as harm the developing brain of the foetus and can also affect the way in which the child develops as it grows.

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

Children whose mothers took VALEPTIC CR during pregnancy have an increased risk of developing autistic spectrum disorders, childhood autism and attention deficit hyperactivity disorder (ADHD).

SCHEDULING STATUS: S3

VALEPTIC CR 300, Controlled release tablets

VALEPTIC CR 500, Controlled release tablets

Sodium valproate

Sugar free

Read all of this leaflet carefully before you start taking VALEPTIC CR

Keep this leaflet. You may need to read it again.

If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

VALEPTIC CR has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What VALEPTIC CR is and what it is used for

2. What you need to know before you take VALEPTIC CR

3. How to take VALEPTIC CR

4. Possible side effects

5. How to store VALEPTIC CR

6. Contents of the pack and other information

1. What VALEPTIC CR is and what it is used for

VALEPTIC CR belongs to a group of medicines called anti-convulsants or anti-epileptics. It is used in the treatment of fits or seizures. It works by controlling the activity of the brain. It is also used to treat certain mental disorders, because of its mood stabilising effect.

Your doctor may therefore prescribe VALEPTIC CR for you:

To treat partial seizures (fits which affect only one part of your brain).

To treat generalized seizures (fits which affect the whole or larger part of your brain and may affect your level of consciousness).

To prevent and treat mania of bipolar disorders (symptoms of great excitement or elation of mood etc. associated with mental illness).

2. What you need to know before you take VALEPTIC CR

Do not take VALEPTIC CR:

- If you are hypersensitive (allergic) to sodium valproate, to peanuts or soya or to any of the other ingredients used in VALEPTIC CR (see section 6)
- If you are breastfeeding your baby (see Pregnancy and Breast-feeding and fertility).
- If you are pregnant:

For the treatment of epilepsy:

- if you are pregnant, unless there is no suitable alternative treatment (see “Pregnancy, breastfeeding and fertility”)

- if you are able to have a baby, unless the conditions of the pregnancy prevention programme are met (see “Pregnancy, breastfeeding and fertility”)

For the treatment of bipolar disorder:

- if you are pregnant
- if you are a woman able to have a baby, unless the conditions of the pregnancy prevention programme are met (see “Pregnancy, breastfeeding and fertility”)

• If you have liver disease such as:

- Inflammation (pain, swelling) of the liver lasting less than six months
- Family history of liver disorders especially if it is due to the use of certain medicines
- Porphyria (enzyme deficiency in the liver that affects the breakdown of components of red blood cells)
- If you have a known metabolic disorder, i.e. a urea cycle disorder
- If you have been told you have a genetic problem caused by a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome).

Warnings and precautions

Take Special care with VALEPTIC CR:

- **If you are a woman or female adolescent able to have a baby:**

If you are a woman or female adolescent that is old enough to become pregnant your doctor should only treat you with VALEPTIC CR if you are not pregnant and you fulfil the requirements of the pregnancy prevention programme. See “Pregnancy and Breastfeeding: Pregnancy: Important information for women”.

If you are taking VALEPTIC CR and you decide you want to start a family, talk to your doctor about this as soon as possible. Do not stop VALEPTIC CR or using birth control (contraception) - until you have been able to discuss this with your doctor. You need to talk to your doctor about the risks for your baby’s health while keeping your illness under control. You and your doctor should agree on what to do with your treatment before you start trying for a baby. See ‘Pregnancy and Breastfeeding: Pregnancy: Important information for women”.

Parents or caregivers of a female (girl) child treated for epilepsy with VALEPTIC CR, must contact the doctor once the female child using VALEPTIC CR experiences her first menstrual period. If you are pregnant, talk to your doctor immediately.

- If you or your child develops a sudden illness, especially if it is within the first six months of treatment, and particularly if it includes repeated vomiting, extreme tiredness, abdominal pain, drowsiness, weakness, loss of appetite, upper stomach pain, nausea, jaundice (yellowing of the skin or whites of the eyes), swelling of the legs or worsening of your epilepsy or a general feeling of being unwell, YOU SHOULD TELL YOUR DOCTOR IMMEDIATELY. VALEPTIC CR can affect the liver (and sometimes the pancreas) in a very small number of patients.
- If you have been told that you have any metabolic disorders, particularly hereditary enzyme deficiency disorders such as a urea cycle disorder where too much ammonia builds up in the body.
- You may be at risk of severe liver damage (see Possible Side Effects):

- You are at greater risk if you are taking more than one anti-convulsant medicine concomitantly.
- Your doctor will carry out regular blood tests and assessments to check your liver function especially during the first six months of your therapy.
- Your doctor will stop therapy if there are any serious abnormalities with your liver function or your dosage will be adjusted accordingly.
- You should report any unusual symptoms to your doctor
- These symptoms include: feelings of weakness, loss of appetite, tiredness, drowsiness, stomach pain or repeated vomiting and recurring fits and spontaneous bruising and bleeding.

- You are also at risk of getting an inflammation (pain, swelling) of the pancreas.
- You may be at greater risk if you get severe seizures or if you have any damage to the brain or nervous system.
- You should tell your doctor if you have any stomach pain and go for a medical evaluation as therapy may need to be stopped if the pancreas is inflamed.

AIso take special care with VALEPTIC CR:

- If you have kidney problems. Your dosage may need to be decreased.
- VALEPTIC CR should only be used in adult males who plan to father a child if alternative treatment options are not suitable.
- If you have systemic lupus erythematosus. This is a disease of the immune system which affects your skin, bones, joints, lungs and kidneys.
- If you have a urea cycle disorder. This causes too much ammonia to build up in your body (see Possible Side Effects).
- If you are gaining weight. This may cause hormonal imbalances and cysts in the ovaries (see Possible Side Effects).
- If you are diabetic. VALEPTIC CR may affect the results of urine tests.
- If you become depressed and have thoughts of harming or killing yourself.
- If your fits get worse or become more frequent you should inform your doctor immediately.
- If you have been told that there is a genetic problem caused by a mitochondrial disorder in your family.
- If you have been told that you have carnitine palmitoyl transferase type II deficiency.

Inform your doctor before treatment if you have any of these conditions.

Other medicines and VALEPTIC CR

Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines.)

These medicines may interact with VALEPTIC CR or VALEPTIC CR may interact with these medicines.

VALEPTIC CR may interact with:

- Neuroleptics (*medicines used to treat mental illnesses*)
- When used in combination with olanzapine (used to treat psychiatric disorders) the following effects may occur: Neutropenia – a blood disorder leading to a reduced chance of fighting

infection, dry mouth, increased appetite and weight gain, problems with speech or sleepiness or extreme tiredness.

- Monoamine oxidase inhibitors or antidepressants (*medicines used to treat depression*)
- Benzodiazepines (*medicines used for anxiety or sleep disorders*)
- Phenobarbital, primidone, phenytoin, carbamazepine and lamotrigine (*medicines used to treat fits or seizures*)
- Zidovudine (*medicines used to treat HIV and AIDS*).
- Propofol (*anaesthetic*)
- Nimodipine – *to treat hypertension*
- Temozolomide – *used to treat cancer*

VALEPTIC CR may increase the blood concentration or activity of these medicines.

Always tell your doctor if you are currently taking any of these medicines so that your dosages may be appropriately adjusted.

- Zidovudine, lopinavir, ritonavir (medicines used to treat AIDS)
- Mefloquine and chloroquine (anti-malarial medicines)
- Aspirin (medicine used to treat pain)
- Warfarin and other coumarin type anti-clotting medicines (medicines used to treat blood clots)
- Cimetidine (medicines used to treat stomach acid or ulcers)
- Erythromycin, rifampicin (antibiotics)
- Carbapenem antibiotics (imipenem/meropenem/ ertapenem/panipenem). The combination of VALEPTIC CR and carbapenems should be avoided because it may decrease the effect of VALEPTIC CR.

- Protease inhibitors (*used to treat HIV*) such as lopinavir and ritonavir
- cholestyramine (*used to treat excessive high blood lipid (fat) levels*)
- acetazolamide (*used to treat glaucoma, seizures or brain swelling*). The combination with VALEPTIC CR may cause a build-up of ammonia in the body

These medicines may affect the blood concentration or activity of VALEPTIC CR thereby increasing your chances of having a fit or seizure.

Always tell your doctor if you are currently taking any of these medicines so that your dosages of VALEPTIC CR may be appropriately adjusted (see How to take VALEPTIC CR).

Other interactions:

VALEPTIC CR does not reduce the effectiveness of oestrogen and/or progesterone containing medicines. VALEPTIC CR does not affect how well the oral contraceptive pill works in women.

VALEPTIC CR with alcohol

Drinking alcohol while taking VALEPTIC CR is not recommended.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.

Important advice for women:

If you are pregnant, you must not use VALEPTIC CR, unless your doctor has determined there is no suitable alternative treatment.

If you are able to have a baby, you must not use VALEPTIC CR unless the conditions of the pregnancy prevention programme are met.

VALEPTIC CR can be harmful to unborn children when taken by a woman during pregnancy. VALEPTIC CR can cause serious birth defects and can affect the way in which the child develops as it grows.

The conditions of the pregnancy prevention programme require that before VALEPTIC CR is prescribed for you:

- your doctor must explain what might happen to your baby if you become pregnant while taking VALEPTIC CR. You need to ensure you understand these risks.

- you will be asked to perform a pregnancy test before starting VALEPTIC CR, or thereafter if needed. This is to make sure you are not pregnant.
- effective birth control (contraception) will be recommended for you to avoid becoming pregnant while taking VALEPTIC CR.
- your doctor will assess your understanding of contraception and the need for contraception without interruption during the entire duration of treatment with VALEPTIC CR.
- your doctor will review your treatment regularly (at least once a year).
- your doctor will ask you to read and sign an “Annual Risk Acknowledgement Form” to make sure you are well aware and have understood all the risks related to the use of VALEPTIC CR during pregnancy and are aware and understand the recommendations to avoid becoming pregnant.
- a Patient Guide will be given to you by your doctor. Make sure you read the Patient Guide that you will receive from your doctor.
- you will also receive a Patient Card from your pharmacist to remind you of the risks of using VALEPTIC CR in pregnancy.

Breastfeeding

VALEPTIC CR passes into the breast milk. You should not breastfeed your baby if you are taking VALEPTIC CR (See “BEFORE YOU TAKE VALEPTIC CR”).

Fertility

VALEPTIC CR can cause infertility in both men and women that may not always be reversible.

Driving and using machines

VALEPTIC CR:

May make you feel sleepy; especially if you are taking it together with other medicines also used to treat fits or medicines used for anxiety or sleep disorders (see Taking other medicines - benzodiazepines).

Make sure you know how you react to VALEPTIC CR before you drive a car, operate tools or machinery, or do anything else that could be dangerous if you are drowsy or light-headed.

It is not always possible to predict to what extent VALEPTIC CR may interfere with the daily activities of a patient. Patients should ensure that they do not engage in driving a vehicle or use machines until they are aware of the measure to which VALEPTIC CR affects them.

VALEPTIC CR contains sodium and lecithin

VALEPTIC CR 300 contains 42 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 2,1 % of the WHO recommended adult maximum daily intake of 2 g sodium.

VALEPTIC CR 500 contains 69 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 3,5 % of the WHO recommended adult maximum daily intake of 2 g sodium.

The daily dose of VALEPTIC CR higher than 3,000 mg is equivalent to 20 % of the WHO recommended adult maximum daily intake of 2 g sodium. This dose is considered high in sodium. This should be taken into account particularly for those on a low sodium diet.

VALEPTIC CR contains soya lecithin (E322). Patients who are allergic to peanut or soya should not use this VALEPTIC CR.

3. HOW TO TAKE VALEPTIC CR

Do not share medicines prescribed for you with any other person.

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

VALEPTIC CR is a controlled release formulation which minimises fluctuations in your blood concentration and ensures a more even concentration throughout the day.

VALEPTIC CR 300 and VALEPTIC CR 500 tablets:

Should be taken orally

Should preferably be taken with or after food

Tablets should be swallowed whole, if necessary with a little water (but not with aerated mineral water)

Tablets should not be crushed or chewed

Your daily dosage requirements may vary according to your age and body weight

Your dose may be prescribed once or twice daily.

The usual dose of VALEPTIC CR in the treatment of epilepsy is:

Adults:

- Your dosage should start at 600 mg/day, in divided doses where applicable
- Your dosage should be increased by 5 to 10 mg/kg/day at weekly intervals until your fits or seizures are controlled
- Your dosage should be within the range of 1 000 to 2 000 mg/day
- Your dosage should be increased in stages, to a maximum of 2 500 mg/day, or one other anti-epileptic medicine may be added at a low dosage
- If you are already receiving other therapy, the same pattern should be followed.
- If you experience increased sedation, then your dosage of barbiturates or benzodiazepines (medicines which treat anxiety) should be reduced as that of VALEPTIC CR is increased.
- If you are taking more than one medicine, then your dosage of both VALEPTIC CR and other medicines used should be adjusted, to give optimum control at the lowest possible dose.

The usual dose of VALEPTIC CR for the treatment and prevention of mania associated with bipolar disorders:

- Your recommended starting dose is 1 000 mg/day
- Your dose should be increased if necessary
- Your dose should be adjusted according to your individual response.

Dosages in special populations:

- ***Patients with kidney impairment:***

Your dosage may need to be reduced.

Your dosage should be adjusted according to your clinical response.

- ***Elderly patients:***

Your dosage should be determined by how well your fits are controlled.

Your doctor will increase the dosage until your condition is controlled. Because of this, it is very important that you follow the instructions your doctor has given you about how much to take. Blood tests may be needed.

Starting therapy with VALEPTIC CR and combination therapy:

- If you are discontinuing other medicines prescribed to control your fits, your dosage of this medicine should be slowly discontinued when you start therapy with VALEPTIC CR.
- Therapy of VALEPTIC CR should then be gradually started, reaching your target dose in two weeks.
- Your dosage of VALEPTIC CR may need to be increased when used in combination with certain medicines used to control fits (e.g., phenytoin, phenobarbitone and carbamazepine)
- Your fits should be controlled with the lowest possible dosage.
- If you are concomitantly taking barbiturates (medicines used to calm you), your dosage of this medicine should be reduced if increased sedation occurs.

If you have the impression that the effect of VALEPTIC CR is too strong or too weak, talk to your doctor or pharmacist.

If you take more VALEPTIC CR than you should

In the event of an overdose, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison centre.

Symptoms of VALEPTIC CR overdose include:

- Drowsiness to deep coma

- Nausea, vomiting, dizziness, unconsciousness
- Low blood pressure, circulatory collapse, shock
- Reduced muscle strength
- Poor reflexes
- Constriction of the pupils of the eyes
- Poor breathing
- Increased pressure inside the skull and swelling of the brain.

Hospital treatment of overdose:

- Your symptoms should be treated
- Your stomach should be washed out
- Your breathing and heart function should be monitored
- You should be put onto a ventilator or other supportive measure if need be
- Your blood should be artificially purified if necessary.

If you missed doses of VALEPTIC CR

Do not take a double dose of VALEPTIC CR to make up for the forgotten individual doses.

If your dosing schedule is:

Once daily: Take your missed dose as soon as possible. Do not double your doses the next day.

Twice daily: Take your missed dose within 6 hours if you remember. Take the other dose for that day at equally spaced intervals. Do not double your dose.

If you stop taking VALEPTIC CR

Do not stop taking or giving your child VALEPTIC CR or alter the dose without checking with your doctor.

4. Possible side effects

VALEPTIC CR can have side effects:

Not all side effects reported for VALEPTIC CR are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking VALEPTIC CR, please consult your healthcare provider for advice.

If any of the following happens, stop taking / using VALEPTIC CR and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to VALEPTIC CR. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

These are very serious side effects of VALEPTIC CR. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent:

- nausea
- vomiting
- abdominal pain
- diarrhoea
- hair loss
- redness
- dizziness
- hearing loss
- headache
- excess of ammonia in blood
- low sodium level in blood
- gingival (gum) problems especially overgrowth
- sore mouth, swollen mouth, mouth ulcers and burning feeling of mouth (stomatitis).
- allergic reactions
- hair loss. When it grows back it may be curlier than before
- impaired water excretion caused by the inability to suppress the secretion of antidiuretic hormone (ADH)
- weight gain (as your appetite may be increased)
- painful periods
- leaking urine by accident
- aggression, agitation, disturbance in attention
- bleeding of excess of blood from damaged blood vessel
- deficiency of platelets in the blood

Less frequent:

- insensibility or extreme tiredness
- rashes with eruptions and redness of the skin
- acne, lowered voice, increased levels of some hormones (androgens), which may lead to increased hair growth on the face, breasts or chest, acne or thinning hair
- tingling or numbness of the hands or feet
- hair, including body and facial hair, grows more than normal in women (polycystic ovarian syndrome)
- impairment of fertility
- menstrual changes (changes in women's period)
- no period or irregular period
- double vision
- inflammation of blood vessel (vasculitis)
- kidney problems such as kidney tubule function that results in excess amounts of glucose, bicarbonate, phosphates (phosphorus salts), uric acid, potassium, and certain amino acids being excreted in the urine, bedwetting or increased need to pass urine, kidney inflammation
- buildup of extra fluid between the layers of lungs (Pleural effusion)
- swelling of the hands and feet
- abnormal behaviour, restlessness/hyperactivity, and learning disorder
- 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.
- breakdown of muscle tissues (Rhabdomyolysis)
- lower number of red blood cells, white blood cells and platelets (pancytopenia)
- decrease in body temperature
- abnormal blood clotting factors

If you notice any side effects of VALEPTIC CR not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get 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 to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of VALEPTIC CR.

5. How to store VALEPTIC CR

Store in a cool, dry place, at or below 25 °C.

Store in the original bottle.

Protect from light. Keep the bottle tightly closed to protect from moisture.

Do not store in a bathroom.

Do not use after the expiry date stated on the carton/bottle.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicines in drains or sewerage systems (e.g., toilets).

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

6. Contents of the pack and other information

What VALEPTIC CR contains

The active ingredient of VALEPTIC CR is: sodium valproate

VALEPTIC CR 300: Each controlled release tablet contains 300 mg sodium valproate.

VALEPTIC CR 500: Each controlled release tablet contains 500 mg sodium valproate.

The other inactive ingredients of VALEPTIC CR are: Copovidone, hypromellose, magnesium stearate, silica, colloidal anhydrous.

PVA based aqueous moisture barrier coating system consisting of the following ingredients: lecithin,

polyvinyl alcohol, talc, titanium dioxide, xanthan gum.

What VALEPTIC CR looks like and contents of the pack

VALEPTIC CR 300:

White or almost white, un-scored and film-coated, round, convex tablet with a diameter of 12,2 – 12,8 mm.

Glass amber bottle with a white aluminium tamper evident screw cap containing 100 tablets. The cap is lined with polyethylene. A white propylene desiccant capsule is added in the container. The amber glass containers are further packed in cardboard boxes pre-printed with the information in accordance with Act 101/1965

VALEPTIC CR 500:

White or almost white unscored and film-coated, capsule tablets with a length of 20,5-21,1 mm and a width of 9,6-10,2 mm.

Glass amber bottle with a white aluminium tamper evident screw cap containing 100 tablets. The cap is lined with polyethylene. A white propylene desiccant capsule is added in the container. The amber glass containers are further packed in cardboard boxes pre-printed with the information in accordance with Act 101/1965.

Holder of Certificate of Registration

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685.

Customer Care: 0860 ADCOCK / 232625

Tel. nr: +27 011 635 0429

This leaflet was last revised in

28 August 2023

Registration numbers

VALEPTIC CR 300: 44/2.5/0067

VALEPTIC CR 500: 44/2.5/0068

adcock ingram

140904-5 06/2024