VELPALEX® IV

VELPALEX IV® has a high teratogenic potential and when used in pregnancy, may cause various major and minor congenital abnormalities of body organs and/or body structures and may also harm the developing brain of the foetus, resulting in cognitive effects in childhood which may include neurodevelopmental disorders such as late walking and talking, poor language skills, memory problems and lower intellectual abilities. Exposure to VELPALEX IV
***in utero* is also associated with an increased risk to develop autistic spectrum disorder, childhood autism and attention deficit hyperactivity disorder (ADHD). VELPALEX IV treatment should be initiated and supervised by a medical practitioner experienced in the treatment of epilepsy or bipolar disorder, and VELPALEX IV should not be prescribed if the relevant risk minimisation measures/pregnancy prevention programme, cannot be implemented and supervised and patients are not committed to adhere to these measures (see sections 4.4 and 4.6).**

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE
VELPALEX® 300 mg IV
VELPALEX® 400 mg IV
VELPALEX® 1 g IV
Solution for infusion or injection (100 mg/mL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
VELPALEX IV contains sodium valproate 100 mg/mL.
Each 3 mL ampoule contains sodium valproate 300 mg.
Each 4 mL ampoule contains sodium valproate 400 mg.
Each 10 mL ampoule contains sodium valproate 1 000 mg.
Sugar free.

Excipient with known effect:
Sodium
VELPALEX 300 mg IV contains 1.93 mmol (44.5 mg) sodium in each 3 mL ampoule.
VELPALEX 400 mg IV contains 2.57 mmol (59.2 mg) sodium in each 4 mL ampoule.
VELPALEX 1 g IV contains 6.44 mmol (148.2 mg) sodium in each 10 mL ampoule.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Solution for infusion or injection.
A clear solution, free from particles.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
In the treatment of generalised epilepsy, particularly with the following patterns of seizures:
- absence
- myoclonic
- tonic-clonic
- atonic
- mixed.

As well as, for partial epilepsy:
- simple or complex seizures
- secondary generalised seizures
- specific syndromes (West, Lennox-Gastaut).

For the treatment and prevention of mania associated with bipolar disorders.
VELPALEX IV is indicated in patients for whom oral therapy is temporarily not possible.

4.2 Posology and method of administration
Posology
Daily dosage requirements vary according to age and body weight. Doses should be adjusted according to individual clinical response.

Adults:
Replace with:
Dosage should start at 600 mg/day, where applicable in divided doses, increasing by 200 mg/day at three-day intervals until control is achieved; this is generally within the range of 1000 - 2000 mg/day (i.e. 20 - 30 mg/kg body mass).
If adequate control has not been achieved after two weeks, the dose may be further increased, in stages, to a maximum of 2 500 mg/day, or one other anti-epileptic medicine may be added as a low dosage. In patients already receiving other therapy, the same pattern should be followed. If increased sedation is observed, dosage of barbiturates or benzodiazepines (e.g. lorazepam) should be reduced as that of VELPALEX IV is increased; dosage of both VELPALEX IV and other medicines should be adjusted during the stabilisation period to give optimum control at the lowest possible combined dosage level, and it may be found possible to maintain optimum control with VELPALEX IV alone.
VELPALEX IV should be replaced by oral valproate therapy as soon as practicable.

Combined therapy:
When starting VELPALEX IV in patients already on other anticonvulsants, these should be tapered slowly. Initiation of VELPALEX IV therapy should then be gradual, with target dose being reached after about 2 weeks. In certain cases, it may be necessary to increase the dose by 5 - 10 mg/kg/day when used in combination with anticonvulsants that induce liver enzyme activity, e.g. phenytoin, phenobarbital (phenobarbitone) and carbamazepine.
Once known enzyme inducers have been withdrawn, or if side effects, such as tremors, are experienced, it may be possible to maintain seizure control on a reduced dose of VELPALEX IV. When barbiturates are being administered concomitantly and particularly if sedation is observed, the dosage of barbiturate should be reduced.

General considerations:
The concentration of valproate in plasma that appears to be associated with therapeutic effects is approximately 30 - 100 micrograms/mL. Optimum dosage is mainly determined by seizure control and routine measurement of plasma levels is unnecessary. However, a method for measurement of plasma levels is available and may be helpful where there is poor control or side effects are suspected (see section 5.2).

Special populations
Elderly patients (65 years and older):
Although the pharmacokinetics of sodium valproate is modified in the elderly, this is of limited clinical significance and dosage should be determined by seizure control and response. The volume of distribution is increased in the elderly, and, because of decreased binding to serum albumin, the proportion of free medicine is increased. This will affect the clinical interpretation of plasma valproic acid levels.

Patients with renal insufficiency:
It may be necessary to decrease the dosage. The dosage should be adjusted according to clinical monitoring, since plasma concentrations may be misleading (see section 5.2).

Bipolar disorders
In children and adolescents:
The safety and efficacy of VELPALEX IV for the treatment of manic episodes in bipolar disorder have not been established in studies in patients aged less than 18 years (sections 4.4 and 4.8).

Patients with hepatic insufficiency:
Refer to sections 4.3, 4.4 and 4.8.

Paediatric population
Children 20 kg and over:
Daily requirement for children is usually in the range of 20 - 30 mg/kg/day and method of administration is as above.
Where adequate control is not achieved within this range, the dose may be increased to 35 mg/kg body mass per day. Above 40 mg/kg/day, clinical chemistry and haematological parameters should be monitored.

Children under 20 kg:
20 mg/kg of body mass per day; in severe cases, this may be increased but only in patients in whom plasma valproic acid levels can be monitored. Above 40 mg/kg/day, clinical chemistry and haematological parameters should be monitored.

Method of administration
VELPALEX IV may be given by direct slow intravenous injection or by infusion. VELPALEX IV should not be administered via the same intravenous line with other IV additives.
VELPALEX IV solution for injection may be given directly by slow intravenous injection, over 3 - 5 minutes, or by infusion using a separate intravenous line in 0.9 % sodium chloride solution for infusion, 5 % dextrose solution for infusion or Ringer's solution for infusion, to achieve a final concentration of 2 mg/mL, see section 6.6.
Prior to use, VELPALEX IV and the diluted solution should be visually inspected. Only clear solutions without particles should be used.
The contents of the ampoule are for single use only. Any remaining solution should be discarded.

4.3 Contraindications
VELPALEX IV is contraindicated in:
- hypersensitivity to sodium valproate or any of the ingredients of VELPALEX IV (see section 6.1)
- active liver disease, including the following:
  - acute hepatitis
  - chronic hepatitis
  - personal or family history of severe hepatitis, especially if medicine-related
  - hepatic porphyria.
- patients known to have mitochondrial disorders caused by mutations in the nuclear gene encoding the mitochondrial enzyme polymerase γ (POLG), e.g., Alpers-Huttenlocher syndrome, and in children under two years of age who are suspected of having a POLG-related disorder (see section 4.4)
- patients with known urea cycle disorders (see section 4.4)
- patients with uncontrolled systemic primary carnitine deficiency (see section 4.4 patients at risk of hyperammonaemia)
- in pregnancy and lactation (see sections 4.4 and 4.6)
- for treatment of epilepsy:
  - in pregnancy unless there is no suitable alternative treatment
  - in women of childbearing potential unless the conditions of the pregnancy prevention programme are fulfilled (see sections 4.4 and 4.6).
- for treatment of bipolar disorder:
  - in pregnancy
  - in women of childbearing potential, unless the conditions of the pregnancy prevention programme are fulfilled.

4.4 Special warnings and precautions for use
Treatment with VELPALEX IV should be initiated and supervised by a medical practitioner experienced in the management of epilepsy and bipolar disorder.
Although there is no specific evidence of sudden recurrence of seizures or underlying symptoms following withdrawal of valproate, discontinuation should normally only be done under the supervision of a specialist in a gradual manner. This is due to the possibility of sudden alterations in plasma concentrations giving rise to a recurrence of symptoms. The generic switching of valproate preparations are not normally recommended due to the clinical implications of possible variations in plasma concentrations.

Women of childbearing potential, female children and pregnant women:
Pregnancy prevention programme
Valproate has a high teratogenic potential and children exposed *in utero* to valproate (as in VELPALEX IV) have a high risk for congenital malformations and neurodevelopmental disorders (see section 4.6).

VELPALEX IV is contraindicated in the following situations:
- in pregnancy unless there is no suitable alternative treatment (see sections 4.3 and 4.6)
- in women of childbearing potential unless the conditions of the pregnancy prevention programme are fulfilled (see sections 4.3 and 4.6).

Conditions of pregnancy prevention programme:
The prescriber must ensure that:
- individual circumstances are evaluated in each case. Involve the patient in the discussion to guarantee her engagement, discuss therapeutic options and ensure her understanding of the risks and the measures needed to minimise the risks
- the potential for pregnancy is assessed for all female patients
- the patient has understood and acknowledged the risks of congenital malformations and neurodevelopmental disorders including the magnitude of these risks for children exposed to valproate *in utero*
- the patient understands the need to undergo pregnancy testing prior to initiation of treatment and during treatment, as needed
- the patient is counselled regarding contraception, and that the patient is capable of complying with the need to use effective contraception (for further details please refer to subsection *Contraception* of this boxed warning), without interruption during the entire duration of treatment with VELPALEX IV
- the patient understands the need for regular (at least annual) review of treatment by a specialist experienced in the management of epilepsy and bipolar disorder
- the patient understands the need to consult her medical practitioner as soon as she is planning pregnancy to ensure timely discussion and switching to alternative treatment options prior to conception and before contraception is discontinued
- the patient understands the need to urgently consult her medical practitioner in case of pregnancy
- the patient has received the patient information leaflet
- the patient has acknowledged that she has understood the hazards and necessary precautions associated with valproate use.

These conditions also concern women who are not currently sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

Female children
The prescriber must ensure that:
- the parents/caregivers of female children understand the need to contact the specialist once the female child using valproate (as in VELPALEX IV) experiences menarche
- the parents/caregivers of female children are fully informed and have been provided with comprehensive information about the risks of congenital malformations and neurodevelopmental disorders including the magnitude of these risks for children exposed to valproate (as in VELPALEX IV) *in utero*.

In patients who have experienced menarche, the prescribing specialist must annually reassess the need for valproate therapy and consider alternative treatment options. If valproate (as in VELPALEX IV) is the only suitable treatment, the need for using effective contraception and all other conditions of the pregnancy prevention programme should be discussed. Every effort should be made by the specialist to switch female children to alternative treatment before they reach adulthood.

Pregnancy test
Pregnancy must be excluded before starting treatment with valproate (as in VELPALEX IV). Treatment with valproate must not be initiated in women of childbearing potential without a negative pregnancy test (plasma pregnancy test) result, confirmed by a healthcare provider, to rule out unintended use in pregnancy.

Contraception
Women of childbearing potential who are prescribed valproate (as in VELPALEX IV) must use effective contraception without interruption during the entire duration of treatment with valproate. These patients must be provided with comprehensive information on pregnancy prevention and should be referred for contraceptive advice if they are not using effective contraception. At least one effective method of contraception (preferably a user independent form such as an intra-uterine device or implant) or two complementary forms of contraception including a barrier method should be used. Individual circumstances should be evaluated in each case when choosing the contraception method, involving the patient in the discussion to guarantee her engagement and compliance with the chosen measures. Even if she has amenorrhoea, she must follow all the advice on effective contraception.

Estrogen-containing products
Concomitant use with estrogen-containing products, including estrogen-containing hormonal contraceptives, may potentially result in decreased valproate (as in VELPALEX IV) efficacy (see section 4.5). Prescribers should monitor clinical response (seizure control) when initiating or discontinuing estrogen-containing products.
Conversely, valproate does not reduce efficacy of hormonal contraceptives.

Annual treatment reviews by a specialist
The specialist should review at least annually whether VELPALEX IV is the most suitable treatment for the patient and ensure that appropriate advice is given and understood by the patient.

Pregnancy planning
If a woman is planning to become pregnant, a specialist experienced in the management of epilepsy must reassess valproate therapy and consider alternative treatment options. Every effort should be made to switch to appropriate alternative treatment prior to conception and before contraception is discontinued (see section 4.6). If switching is not possible, the woman should receive further counselling regarding the risks of valproate for the unborn child to support her informed decision-making regarding family planning.

Bipolar disorder
If a woman is planning to become pregnant, a medical practitioner experienced in the management of bipolar disorder must be consulted and treatment with VELPALEX IV should be discontinued and, if needed, switched to an alternative treatment prior to contraception and before contraception is discontinued. VELPALEX IV is not indicated for the treatment of manic episodes in bipolar disorder in children (section 4.1).

In case of pregnancy
If a woman using valproate (as in VELPALEX IV) becomes pregnant, she must be immediately referred to a specialist to re-evaluate treatment with valproate and consider alternative treatment options. The patients with valproate-exposed pregnancy and their partners should be referred to a specialist experienced in prenatal medicine for evaluation and counselling regarding the exposed pregnancy (see section 4.6).

Pharmacists must ensure that:
The Patient Information Leaflet is provided with every valproate dispensation and that patients understand its content.
Patients are advised not to stop VELPALEX IV and to immediately contact a specialist in case of planned or suspected pregnancy.
Sodium valproate therapy should only be continued after a reassessment of the benefits and risks of the treatment with valproate for the patient by a specialist experienced in the management of epilepsy.

Use in male patients
A retrospective observational study suggests an increased risk of neuro-developmental disorders (NDDs) in children born to men treated with valproate in the 3 months prior to conception compared to those born to men treated with lamotrigine or levetiracetam (see section 4.6).

As a precautionary measure, medical practitioners should inform male patients about this potential risk (see section 4.6) and discuss the need to consider effective contraception, including for a female partner, while using valproate and for at least 3 months after treatment discontinuation. Male patients should not donate sperm during treatment and for at least 3 months after treatment discontinuation.

Male patients treated with VELPALEX IV should be regularly reviewed by their medical practitioner to evaluate whether VELPALEX IV treatment is the most suitable for the patient. For male patients planning to conceive a child, suitable treatment alternatives should be considered and discussed with the male patients. Individual circumstances should be evaluated in each case. It is recommended that advice from a medical practitioner experienced in the management of epilepsy or bipolar disorder should be sought as appropriate.

Educational materials are available for health care providers and male patients. A patient guide should be provided to male patients using valproate.

Liver dysfunction:
Conditions of occurrence:
Severe liver damage, including hepatic failure sometimes resulted in fatalities, have been reported. Experience in epilepsy has indicated that patients most at risk, especially in cases of multiple anticonvulsant therapy, are infants and in particular young children under the age of 3 years and those with severe seizure disorders, organic brain disease, and (in) congenital metabolic or degenerative disease associated with mental retardation. After the age of 3 years, the incidence of occurrence is significantly reduced and progressively decreases with age.
The concomitant use of salicylates should be avoided in children under 3 years due to the risk of liver toxicity. Additionally, salicylates should not be used in children under 16 years (see aspirin/salicylate product information on Reye's syndrome).
Monotherapy is recommended in children under the age of 3 years when prescribing VELPALEX IV, but the potential benefit of VELPALEX IV should be weighed against the risk of liver damage or pancreatitis in such patients prior to initiation of therapy.
In most cases, such liver damage occurred during the first 6 months of therapy.

Suggestive signs:
Clinical symptoms are essential for early diagnosis. In particular the following conditions, which may precede jaundice, should be taken into consideration, especially in patients at risk (see above, Conditions of occurrence):
- non-specific symptoms, usually of sudden onset, such as asthenia, malaise, anorexia, lethargy, oedema and drowsiness, which are sometimes associated with repeated vomiting and abdominal pain.
- in patients with epilepsy, recurrence of seizures:

These are an indication for immediate withdrawal of the medicine.
Patients or their family, in the case of children) should be instructed to immediately report any such signs to a medical practitioner should they occur. Investigations including clinical examination and biological assessment of liver function should be undertaken immediately.

Detection:
Liver function should be measured before therapy and then periodically monitored during the first 6 months of therapy, especially in those who seem most at risk, and those with a prior history of liver disease.
Amongst usual investigations, tests which reflect protein synthesis, particularly prothrombin rate, are most relevant.
Confirmation of an abnormally low prothrombin rate, particularly in association with other biological abnormalities (including significant decrease in fibrinogen and coagulation factors; increased bilirubin level and raised transaminases) requires cessation of VELPALEX IV therapy.
As a matter of precaution and in case they are taken concomitantly, salicylates should also be discontinued since they employ the same metabolic pathway.
Increased liver enzymes are common, particularly at the beginning of therapy; they are also transient.
More extensive biological investigations (including prothrombin rate) are recommended in these patients; a reduction in dosage may be considered when appropriate and tests should be repeated as necessary.

Pancreatitis:
Pancreatitis, which may be severe and result in fatalities, has been reported. Patients experiencing nausea, vomiting or acute abdominal pain should have a prompt medical evaluation (including measurement of serum amylase). Young children are at particular risk; this risk decreases with increasing age. Severe seizures and severe neurological impairment with combination anticonvulsant therapy may be risk factors. Hepatic failure with pancreatitis increases the risk of fatal outcome. In case of pancreatitis, VELPALEX IV should be discontinued.

Aggravated convulsions:
Some patients may experience, instead of an improvement, a reversible worsening of convulsion frequency and severity in conjunction with status epilepticus, or the onset of new types of convulsions with valproate (as in VELPALEX IV). In case of aggravated convulsions, the patients should be advised to consult their medical practitioner immediately (see section 4.8).

Suicidal ideation and behaviour:
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic medicines in several indications. Studies show a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known, and the available data does not exclude the possibility of an increased risk for sodium valproate (as in VELPALEX IV).
Therefore, patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

Carbapenem medicines:
The concomitant use of valproate and carbapenem medicines is not recommended.

Patients with known or suspected mitochondrial disease:
VELPALEX IV may trigger or worsen clinical signs of underlying mitochondrial diseases caused by mutations of mitochondrial DNA as well as the nuclear encoded POLG gene. In particular, valproate-induced liver-related deaths have been reported at a higher rate in patients with hereditary neurometabolic syndromes caused by mutations in the gene for the mitochondrial enzyme polymerase γ (POLG), e.g. Alpers-Huttenlocher syndrome. POLG-related disorders should be suspected in patients with a family history or suggestive symptoms of a POLG-related disorder, including but not limited to unexplained encephalopathy, refractory epilepsy (focal, myoclonic), status epilepticus at presentation, developmental delays, psychomotor regression, axonal sensorimotor neuropathy, myopathy, cerebellar ataxia, ophthalmoplegia, or complicated migraine with cortical aura. POLG mutation testing should be performed in accordance with current clinical practice for the diagnostic evaluation of such disorders (see section 4.3).

Haematological tests:
Blood tests (blood cell count, including platelet count, bleeding time and coagulation tests) are recommended prior to initiation of therapy or before surgery, and in case of spontaneous bruising or bleeding (see section 4.8).

Renal insufficiency:
In patients with renal insufficiency, it may be necessary to decrease dosage. As monitoring of plasma concentration may be misleading, dosage should be adjusted according to clinical monitoring (see sections 4.2 and 5.2).

Patients with systemic lupus erythematosus (SLE):
Although immune disorders have not only rarely been noted during the use of VELPALEX IV, the potential benefit of VELPALEX IV should be weighed against its potential risk in patients with systemic lupus erythematosus (see also section 4.8). New development and exacerbation of SLE may occur.

Urea cycle disorders:
When a urea cycle enzymatic deficiency is suspected, metabolic investigations should be performed prior to treatment because of the risk of hyperammonaemia with VELPALEX IV (see section 4.3).

Weight gain:
VELPALEX IV frequently causes weight gain, which may be marked and progressive. Patients should be warned of the risk of weight gain at the initiation of therapy and appropriate strategies should be adopted to minimise it (see section 4.8).

Diabetic patients:
VELPALEX IV is eliminated mainly through the kidneys, partly in the form of ketone bodies; this may give false positives in the urine testing of diabetics.

Patients at risk of hypocarnitinaemia:
VELPALEX IV administration may trigger occurrence or worsening of hypocarnitinaemia that can result in hyperammonaemia (that may lead to hyperammonaemic encephalopathy). Other symptoms such as liver toxicity, hypoketotic hypoglycaemia, myopathy including cardiomyopathy, rhabdomyolysis, Fanconi syndrome have been observed, mainly in patients with risk factors for hypocarnitinaemia or pre-existing hypocarnitinaemia. Valproate may decrease carnitine blood and tissue levels and therefore impair mitochondrial metabolism including the mitochondrial urea cycle. Patients at increased risk for symptomatic hypocarnitinaemia when treated with VELPALEX IV include patients with metabolic disorders, including mitochondrial disorders related to carnitine (see warnings on Patients with known or suspected mitochondrial disease and Urea cycle disorders above and risk of hyperammonaemia), impairment in carnitine nutritional intake, patients younger than 10 years old, concomitant use of pivalate-conjugated medicines or of other antiepileptics.
Patients should be warned to immediately report any signs of hyperammonaemia such as ataxia, impaired consciousness, vomiting for further investigation. Carnitine supplementation should be considered when symptoms of hypocarnitinaemia are observed.
Patients with systemic primary carnitine deficiency and corrected for hypocarnitinaemia should be treated with VELPALEX IV only if the benefits of VELPALEX IV treatment outweigh the risks in these patients and there is no suitable therapeutic alternative. In these patients, close monitoring for recurrence of hypocarnitinaemia should be implemented.
Patients with an underlying carnitine palmitoyltransferase (CPT) type II deficiency should be warned of the greater risk of rhabdomyolysis when taking VELPALEX IV.

Alcohol:
Alcohol intake is not recommended during treatment with valproate.

Adult males intending procreation:
Valproate, as contained in VELPALEX IV, has been associated with male fertility dysfunction that may not always be reversible after treatment discontinuation (see sections 4.6 and 4.8). The medical practitioner should discuss with adult males their intent to procreate, when prescribing VELPALEX IV. If procreation is intended, VELPALEX IV should be used only if alternative treatment options are not available.

VELPALEX IV contains sodium (see section 2).
VELPALEX 300 mg IV contains 1.93 mmol (44.5 mg) sodium in each 3 mL ampoule. This is equivalent to 2 % of the recommended maximum daily dietary intake of 2 g sodium for an adult.
VELPALEX 400 mg IV contains 2.57 mmol (59.2 mg) sodium in each 4 mL ampoule. This is equivalent to 3 % of the recommended maximum daily dietary intake of 2 g sodium for an adult.
VELPALEX 1 g IV contains 6.44 mmol (148.2 mg) sodium in each 10 mL ampoule. This is equivalent to 7 % of the recommended daily dietary intake of 2 g sodium for an adult.

Paediatric population
Children (male and female) less than 18 years of age:
Some psychiatric disorders, including aggression, agitation, disturbance in attention, abnormal behaviour, psychomotor hyperactivity and cognitive impairment, may be observed in paediatric patients receiving VELPALEX IV (see section 4.8). Current evidence is inconclusive as to the possibility of harm to reproductive organs, skeletal system growth or developing brain of patients less than 18 years of age.
In male children less than 18 years of age, VELPALEX IV should be used with caution and in alignment with guidelines in so suitable alternative treatment is available.
VELPALEX IV can be used in female children less than 18 years of age only if there is no suitable safer alternative therapy or alternate therapy have failed to control the epilepsy. In addition, for female children, ensure that the conditions of the pregnancy prevention programme are met (see section 4.4 and 4.6).

4.5 Interaction with other medicines and other forms of interaction
Effects of VELPALEX IV on other medicines
Antipsychotics, MAO inhibitors, antidepressants and benzodiazepines
VELPALEX IV may potentiate the effect of other psychotropics such as antipsychotics, MAO inhibitors, antidepressants and benzodiazepines; therefore, clinical monitoring is advised and the dosage of the other psychotropics should be adjusted when appropriate.
In particular, a clinical study has suggested that adding olanzapine to valproate or lithium therapy may significantly increase the risk of certain adverse events associated with olanzapine (e.g. neutropenia, tremor, dry mouth, increased appetite and weight gain, speech disorder and somnolence.

Lithium
VELPALEX IV has no effect on serum lithium levels.

Olanzapine
Valproic acid (as in VELPALEX IV) may decrease the olanzapine plasma concentration.

Phenobarbital
VELPALEX IV increases phenobarbital plasma concentrations (due to inhibition of hepatic catabolism) and sedation may occur, particularly in children. Therefore, clinical monitoring is recommended throughout the first 15 days of combined treatment with immediate reduction of phenobarbital doses if sedation occurs and determination of phenobarbital plasma levels when appropriate.

Primidone
VELPALEX IV increases primidone plasma levels with exacerbation of its adverse effects (such as sedation); these signs cease with long-term treatment. Clinical monitoring is recommended especially at the beginning of combined therapy with dosage adjustment when appropriate.

Phenytoin
VELPALEX IV decreases phenytoin total plasma concentration. Moreover, VELPALEX IV increases phenytoin free form with possible overdose symptoms (valproic acid displaces phenytoin from its plasma protein binding sites and reduces its hepatic catabolism). Therefore, clinical monitoring is recommended; when phenytoin plasma levels are determined, the free form should be evaluated.

Carbamazepine
Clinical toxicity has been reported when VELPALEX IV was administered with carbamazepine as VELPALEX IV may potentiate toxic effects of carbamazepine. Clinical monitoring is recommended especially at the beginning of combined therapy with dosage adjustment when appropriate.

Lamotrigine
VELPALEX IV reduces the metabolism of lamotrigine and increases the lamotrigine mean half-life by nearly two-fold. This interaction may lead to increased lamotrigine toxicity, in particular serious skin rashes. Therefore, clinical monitoring is recommended, and dosages should be adjusted (lamotrigine dosage decreased) when appropriate.

Felbamate
Valproic acid may decrease the felbamate mean clearance by up to 16 %.

Rufinamide
Valproic acid may lead to an increase in plasma levels of rufinamide. This increase is dependent on concentration of valproic acid. Caution should be exercised, in particular in children, as this effect is larger in this population.

Propofol
Valproic acid may lead to an increased blood level of propofol. When co-administered with valproate, a reduction of the dose of propofol should be considered.

Zidovudine
VELPALEX IV may raise zidovudine plasma concentration leading to increased zidovudine toxicity.

Nimodipine
In patients concomitantly treated with VELPALEX IV and nimodipine the exposure to nimodipine can be increased by 50 %. The nimodipine dose should therefore be decreased in case of hypotension.

Temozolomide
Co-administration of temozolomide and VELPALEX IV may cause a small decrease in the clearance of temozolomide that is not thought to be clinically relevant.

Effects of other medicines on VELPALEX IV
Anti-epileptics
Anti-epileptics with enzyme inducing effect (including phenytoin, phenobarbital, carbamazepine) decrease valproic acid plasma concentrations. Dosages should be adjusted according to clinical response and blood levels in case of combined therapy.
Valproic acid metabolite levels may be increased in the case of concomitant use with phenytoin or phenobarbital. Therefore, patients treated with those two medicines should be carefully monitored for signs and symptoms of hyperammonaemia.
On the other hand, combination of felbamate and VELPALEX IV decreases valproic acid clearance by 22 - 50 % and consequently increase the valproic acid plasma concentrations. VELPALEX IV dosage should be monitored.

Anti-malarial medicines
Mefloquine and chloroquine increase valproic acid metabolism and may lower the seizure threshold; therefore, epileptic seizures may occur in cases of combined therapy. Accordingly, the dosage of VELPALEX IV may need adjustment.

Highly protein bound medicines
In case of concomitant use of VELPALEX IV and highly protein bound medicines (e.g. aspirin), free valproic acid plasma levels may be increased.

Vitamin K-dependent factor anticoagulants
The anticoagulant effect of warfarin and other coumarin anticoagulants may be increased following displacement from plasma protein binding sites by valproic acid. The prothrombin time should be closely monitored.

Cimetidine or erythromycin
Valproic acid plasma levels may be increased (as a result of reduced hepatic metabolism) in case of concomitant use with cimetidine or erythromycin.

Carbapenem antibiotics (such as panipenem, imipenem and meropenem)
Decreases in blood levels of valproic acid have been reported when it is co-administered with carbapenem medicines resulting in a 60 - 100 % decrease in valproic acid levels within two days, sometimes associated with convulsions. Due to the rapid onset and the extent of the decrease, co-administration of carbapenem medicines in patients stabilised on valproic acid (as in VELPALEX IV) should be avoided (see section 4.4). If treatment with these antibiotics cannot be avoided, close monitoring of valproic acid blood levels should be performed.

Rifampicin
Rifampicin may decrease the valproic acid blood levels resulting in a lack of therapeutic effect. Therefore, valproate dosage adjustment may be necessary when it is co-administered with rifampicin.

Protease inhibitors
Protease inhibitors such as lopinavir and ritonavir decrease valproate plasma level when co-administered with VELPALEX IV. Although formal interaction studies have not been performed, available data suggest a reduction ranging from 40 % to 77.5 % in valproate plasma levels. Although protease inhibitors such as ritonavir for the treatment of HIV infection should be carefully monitored for decreased control of their epilepsy/mood status of bipolar patients if also treated with VELPALEX IV.

Colestyramine
Colestyramine may lead to a decrease in plasma level of valproate when co-administered with VELPALEX IV.

Estrogen-containing products, including estrogen-containing hormonal contraceptives
Estrogens are inducers of the UDP-glucuronosyl transferase (UGT) isoforms involved in valproate glucuronidation and may increase the clearance of valproate, which would result in decreased serum concentration and potentially decreased valproate efficacy (see section 4.4). Consider monitoring of valproate serum levels.
Conversely, valproate has no enzyme inducing effect, as a consequence, valproate does not reduce efficacy of estroprogestative medicines in women receiving hormonal contraception.

Metamizole
Metamizole may decrease valproate serum levels when co-administered, which may result in potentially decreased valproate clinical efficacy. Precautions should monitor clinical response (seizure control) and consider monitoring valproate serum levels as appropriate.

Methotrexate
Some case reports describe a significant decrease in valproate serum levels after methotrexate administration, with occurrence of seizures. Medical practitioners should monitor clinical response (seizure control or mood control) and consider monitoring valproate serum levels as appropriate.

Other interactions
Risk of liver damage
The concomitant use of salicylates should be avoided in children under 3 years of age due to the risk of liver toxicity (see section 4.4). Concomitant use of VELPALEX IV and multiple anticonvulsant therapy increases the risk of liver damage, especially in young children (see section 4.4).
In patients of all ages receiving cannabidiol at doses 10 to 25 mg/kg and valproate concomitantly, clinical trials have reported ALT increases greater than 3 times the upper limit of normal in 19 % of patients.
Appropriate liver monitoring should be exercised when VELPALEX IV is used concomitantly with other anticonvulsants with potential hepatotoxicity, including cannabidiol, and dose reductions or discontinuation should be considered in case of significant anomalies of liver parameters (see section 4.4).

Topiramate and acetazolamide
Caution is advised when using VELPALEX IV in combination with newer anti-epileptics whose pharmacodynamics may not be well established.
Concomitant administration of valproate and topiramate or acetazolamide has been associated with encephalopathy and/or hyperammonaemia. In patients taking these two medicines, careful monitoring of signs and symptoms is advised particularly in at risk patients such as those with pre-existing encephalopathy.

Pivalate-conjugated medicines
Concomitant administration of VELPALEX IV and pivalate-conjugated medicines that decrease carnitine levels (such as cefotetan pivoxil, adefovir dipivoxil, pivmecillinam and pivampicillin) may trigger occurrence of hypocarnitinaemia (see section 4.4: Patients at risk of hypocarnitinaemia). Concomitant administration of these medicines with VELPALEX IV is not recommended. Patients in whom coadministration cannot be avoided should be carefully monitored for signs and symptoms of hypocarnitinaemia.

Quetiapine
Co-administration of VELPALEX IV and quetiapine may increase the risk of neutropenia/ leucopenia.

Estrogen- and/or progestogen-containing medicines
VELPALEX IV usually has no enzyme-inducing effect. As a consequence, VELPALEX IV does not reduce efficacy of estrogen-and/or progestogen-containing medicines in women receiving hormonal contraception.

4.6 Fertility, pregnancy and lactation
Pregnancy

Treatment of epilepsy
VELPALEX IV is contraindicated in pregnancy and lactation (see section 4.3).
VELPALEX IV should not be used in female children, in female adolescents, in women of childbearing potential and in pregnant women unless other treatments are ineffective or not tolerated (see sections 4.3, 4.4).
VELPALEX IV is contraindicated in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled.

Treatment of bipolar disorder
VELPALEX IV is contraindicated during pregnancy.
VELPALEX IV in women of childbearing potential, unless the conditions of the Pregnancy Prevention Programme are fulfilled (see sections 4.3 and 4.4).

Both valproate monotherapy and valproate polytherapy including other anti-epileptics are frequently associated with abnormal pregnancy outcomes. Available data suggest that anti-epileptic polytherapy including valproate may be associated with a greater risk of congenital malformations than valproate monotherapy.

Congenital malformations
In offspring born to mothers with epilepsy receiving any anti-epileptic treatment, the global rate of malformations has been demonstrated to be 2 - 3 times higher than the rate (approximately 3 %) reported in the general population. Although an increased incidence of cleft lip and palate malformations have been reported in case of multiple medicine therapy, the respective part of treatments and disease has not been formally established.
Available data show an increased incidence of minor and major malformations. The most common types of malformations include neural tube defects, facial dysmorphism, cleft lip and palate, craniostenosis, cardiac, renal and urogenital defects, limb defects (including bilateral aplasia of the radius), and multiple anomalies involving various body systems.
In utero exposure to valproate may also result in hearing impairment or deafness due to ear and/or neurological malformations (secondary effects) and/or direct toxicity on the hearing function. Cases describe both unilateral and bilateral deafness or hearing impairment. Outcomes were not reported for all cases. When outcomes were reported, the majority of cases did not recover.
In utero exposure to valproate may result in eye malformations (including coloboma, microphthalmia) that have been reported in conjunction with other congenital malformations.

Developmental problems/neurodevelopmental disorders
Data have shown that exposure to valproate *in utero* can have adverse effects on mental and physical development of the exposed children. The risk seems to be dose-dependent, but a threshold dose below which no risk exists, cannot be established based on available data. The exact gestational period of risk for these effects is uncertain and the possibility of a risk throughout the entire pregnancy cannot be excluded.
Developmental problems have been reported in up to 30 - 40 % of pre-school children exposed to valproate (as contained in VELPALEX IV) *in utero*, including delays in early development such as walking and talking later, lower intellectual abilities, poor language skills (speaking and understanding) and memory problems.
Children exposed to valproate in the womb are also at increased risk of autistic spectrum disorder (around 3 times higher than in the general population) and childhood autism (up to 5 times higher than in the general population). There are also limited data suggesting that children exposed to valproate in the womb may be more likely to develop symptoms of attention deficit hyperactivity disorder (ADHD).

Other risks in the neonate
Haemorrhagic syndrome has been reported in neonates whose mothers have taken VELPALEX IV during pregnancy. This haemorrhagic syndrome is related to thrombocytopenia, hypofibrinogenaemia and/or to decreases in other coagulation factors; afibrinogenaemia has also been reported and may be fatal. However, this coagulopathy must be distinguished from the decrease of the vitamin K factors induced by phenobarbital and other anti-epileptic enzyme inducing medicines.
Therefore, platelet count, fibrinogen plasma level, coagulation tests and coagulation factors should be investigated in neonates.
Cases of hypoglycaemia have been reported in neonates, whose mothers have taken valproate (as in VELPALEX IV) during the third trimester of the pregnancy.
Cases of hypothyroidism have been reported in neonates whose mothers have received valproate (as in VELPALEX IV) during pregnancy.
Withdrawal symptoms may occur, in particular, agitation, irritability, hyper-excitability, jitteriness, hyperkinesia, toniclty disorders, tremor, convulsions and feeding disorders) may occur in neonates whose mothers have taken valproate during the last trimester of their pregnancy.

Female children and woman of childbearing potential (see above and section 4.4)

If a woman plans a pregnancy
If a woman is planning to become pregnant, a specialist experienced in the management of epilepsy must reassess valproate therapy and consider alternative treatment options. Every effort should be made to switch to appropriate alternative treatment prior to conception and before contraception is discontinued (see section 4.4). If switching is not possible, the woman should receive further counselling regarding the risks of valproate for the unborn child to support her informed decision-making regarding family planning.

Pregnant women
Valproate as treatment for epilepsy is contraindicated in pregnancy unless there is no suitable alternative treatment (see sections 4.3 and 4.4). If a woman using valproate becomes pregnant, she must be immediately referred to a specialist to consider alternative treatment options.

During pregnancy, maternal tonic clonic seizures and status epilepticus with hypoxia may carry a particular risk of death for the mother and the unborn child. If in exceptional circumstances, despite the known risks of valproate in pregnancy and after careful consideration of alternative treatment, a pregnant woman must receive valproate for epilepsy, it is recommended to:
- use the lowest effective dose and divide the daily dose of valproate into several small doses to be taken throughout the day
- the use of a prolonged release formulation may be preferable to other treatment formulations in order to avoid high peak plasma concentrations.

All patients with valproate-exposed pregnancy and their partners should be referred to a specialist experienced in prenatal medicine for evaluation and counselling regarding the exposed pregnancy. Specialised prenatal monitoring should take place to detect the possible occurrence of neural tube defects or other malformations. Folate supplementation before the pregnancy may reduce the risk of ne

PATIENT INFORMATION LEAFLET

Valproate, as in VELPALEX® IV, may cause birth defects and problems with early development of the child if it is given during pregnancy. If you are a female of childbearing age, you should use an effective method of contraception throughout your treatment (see Pregnancy, breastfeeding and fertility). Tell your doctor at once if you want to become pregnant or think you might be pregnant. If you are the parent or caregiver of a female child being treated with VELPALEX IV, read the section on pregnancy, breastfeeding and fertility in this leaflet carefully.

SCHEDULING STATUS: S3

VELPALEX® 300 mg IV
VELPALEX® 400 mg IV
VELPALEX® 1 g IV
Solution for infusion or injection (100 mg/mL)
Sodium valproate
Sugar free
Contains sodium: 44,5 mg/3 mL; 59,2 mg/4 mL and 148,2 mg/10 mL

Read all of this leaflet carefully before you are given VELPALEX IV
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet
1. What VELPALEX IV is and what it is used for
2. What you need to know before you are given VELPALEX IV
3. How VELPALEX IV will be administered
4. Possible side effects
5. How VELPALEX IV will be stored
6. Contents of the pack and other information

1. WHAT VELPALEX IV is and what it is used for

VELPALEX IV contains sodium valproate, which belongs to a group of medicines called anti-epileptics. These are used to control epileptic seizures. VELPALEX IV solution for injection is used to treat various types of epileptic seizures (fits) when it is not possible to take sodium valproate tablets.

VELPALEX IV is also used in mania: where you may feel excited, elated, agitated, enthusiastic or hyperactive. Mania occurs in an illness called "bipolar disorder".

2. What you need to know before you are given VELPALEX IV

VELPALEX IV should not be administered to you or your child, if you:
- are hypersensitive (allergic) to sodium valproate or any of the ingredients of VELPALEX IV (listed in section 6)
- have liver problems, or have a family history of liver problems
- suffer from porphyria (a rare condition that affects the breakdown of components of red blood cells)
- have a genetic problem causing a mitochondrial disorder (e.g. Alpers-Huttenlocher syndrome)
- suffer from urea cycle disorder (a certain metabolic disorder)
- are pregnant or able to have a baby:
  - for the treatment of epilepsy:
    - if you or female (girl) child is pregnant, unless there is no suitable alternative treatment (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women)
    - if you or your female (girl) child is able to have a baby, unless the conditions of the Pregnancy Prevention Programme are met (see Pregnancy, breastfeeding and fertility: Pregnancy – Important information for women)
  - 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 – Important information for women)
- have an inborn carnitine deficiency (a very rare metabolic disease) that is untreated.

Warnings and precautions
Talk to your doctor or healthcare provider before you are given VELPALEX IV, if you:
- have diabetes. VELPALEX IV may affect the results of urine tests
- have a carnitine palmitoyltransferase type II deficiency, which prevents the body from using certain fats for energy, as you may be more prone to serious side effects
- have kidney problems. Your doctor may give you a lower dose
- have a brain disease or a metabolic condition affecting your brain
- have a 'urea cycle disorder' where too much ammonia builds up in the body
- have an illness called 'systemic lupus erythematosus (SLE)' – a disease of the immune system which affects skin, bones, joints and internal organs
- 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 receiving VELPALEX IV
- are having surgery, including dental surgery, tell the doctor or dentist that you are receiving VELPALEX IV. You will need to take extra care in cleaning your teeth to prevent infection, as side effects of VELPALEX IV include bleeding and swelling of the gums (see section 4).

Liver damage
VELPALEX IV may cause severe and life-threatening damage to your liver. Signs that you may notice include seizures that are becoming more severe or happen more often, or excessive tiredness, lack of energy, weakness, stomach pain, loss of appetite, nausea, vomiting, yellow skin and eye whites or swelling of the face. Tell your doctor immediately if you notice these symptoms. The risk of liver damage is increased if your child is less than 3 years of age, and who is taking other anti-epileptic medicines at the same time as VELPALEX IV or has other neurological or metabolic diseases and severe forms of epilepsy.

If your child is under 3 years of age, VELPALEX IV should not be administered together with aspirin.

Pancreas damage
VELPALEX IV may cause serious or life-threatening damage to the pancreas. This may occur at any time during treatment. If you experience any of the following symptoms, tell your doctor immediately: stomach pain, nausea, vomiting, or loss of appetite.

Suicidal thoughts and behaviour
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.
There may also be a risk that you will experience changes in your mental health if your condition is not treated.

Convulsions
Convulsions may become worse or happen more frequently while taking this medicine. If this happens contact your doctor immediately.

Weight gain
Receiving VELPALEX IV 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 are given VELPALEX IV and during your treatment.

Carnitine palmitoyl transferase type II deficiency
If you or your child has been told that you have carnitine palmitoyl transferase type II deficiency.

Bipolar disorder
VELPALEX IV should not be used for the treatment of mania associated with bipolar disorders in children and adolescents under the age of 18 years.

Children and adolescents
While treated with VELPALEX IV, do not give salicylates (aspirin) to children under 3 years due to the risk of liver toxicity. Additionally, do not use salicylates in children under 16 years as it can increase the risk of Reye's syndrome (an acute condition that causes swelling in the brain and liver).

Children (male and female) less than 18 years of age:
VELPALEX IV should be used with caution in male and female children under the age of 18 years, for the treatment of epilepsy.
For female children, ensure that the conditions of the pregnancy prevention programme are met.
Some psychiatric disorders, including aggression, agitation, disturbance in attention, abnormal behaviour, psychomotor hyperactivity and learning disorder, may be observed in paediatric patients receiving VELPALEX IV (see Possible side effects). Current evidence is inconclusive as to the possibility of harm to reproductive organs, skeletal system growth or developing brains of patients less than 18 years of age.

Other medicines and VELPALEX IV
Always tell your healthcare provider if you are taking any other medicine. This includes complementary or traditional medicines.

The following medicines can increase the chance of you getting side effects, when given with VELPALEX IV:
- some medicines used for pain and inflammation (salicylates) such as aspirin
- some other medicines used to treat fits – see section 3. Patients taking other medicines for fits (epilepsy). This includes medicines such as phenobarbital, primidone, phenytoin, carbamazepine, rufinamide, topiramate, lamotrigine and felbamate
- acetazolamide, used to treat glaucoma or fits. The combination with VELPALEX IV may cause a build-up of ammonia in the body.

VELPALEX IV injection may increase the effect of the following medicines:
- medicines for depression, for example, monoamine oxidase inhibitors (MAOI) such as moclobemide, selegiline
- medicines used to calm emotional and mental health problems (including schizophrenia, bipolar disorder and depression) such as quetiapine, olanzapine, olanzapine and lithium
- propofol – used for anaesthesia
- zidovudine used to treat HIV infection
- nimodipine (used to decrease problems due to a certain type of bleeding in the brain)
- temozolomide used to treat cancer
- medicines used to thin the blood (such as warfarin).

The following medicines can affect the way VELPALEX IV works:
- some medicines used for the prevention and treatment of malaria such as mefloquine and chloroquine
- cimetidine used for stomach ulcers
- antibiotics e.g. ethynromycin, carbapenems (antibiotics used to treat bacterial infections). The combination of valproate and carbapenems should be avoided because it may decrease the effect of sodium valproate
- rifampicin used to treat tuberculosis and other infections
- protease inhibitors such as lopinavir and ritonavir – used for HIV infection and AIDS
- colestyramine used to lower blood fat (cholesterol) levels. It may still be possible for you to be given VELPALEX IV, your doctor will advise you on what is suitable for you
- hormonal contraceptive products (including pills)
- mefamizole, a pain killer, may reduce the effect of VELPALEX IV
- methotrexate (used to treat cancer and inflammatory diseases)
- some anti-infectives that contain pivalate (e.g. pivampicillin, adefovir dipivoxil)
- cannabidiol (commonly known as CBD used in epilepsy and other conditions).

Using VELPALEX IV with food and drink
Alcohol intake is not recommended during treatment.
You should not drink alcoholic drinks while you are treated with VELPALEX IV.

Pregnancy, breastfeeding and fertility

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

Pregnancy

If you are pregnant, you should not be given VELPALEX IV, unless other treatments are not effective or well tolerated.
Do not stop receiving VELPALEX IV without consulting your doctor as doing so could cause harm to you or an unborn child.
If you are a woman able to have a baby, you must not receive VELPALEX IV unless you use an effective method of birth control (contraception) during your entire treatment with VELPALEX IV. Speak to your doctor if you have any questions about which contraceptive method is appropriate for you.
VELPALEX IV can cause malformation and problems with early development of children if they are exposed to valproates in the womb.

VELPALEX IV can cause serious birth defects and can affect the way in which the child develops as it grows. Birth defects which have been reported include spina bifida (where the bones of the spine are not properly developed); facial and skull malformations; heart, kidney, urinary tract and sexual organ malformations; limb defects.
Hearing problems or deafness have been reported in children exposed to valproate during pregnancy.

It is estimated that up to 30 - 40 % of preschool children whose mothers took sodium 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 sodium 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 VELPALEX IV. If you decide later, you want to have a child you should not stop taking your medicine or your method of birth control (contraception) until you have discussed this with your doctor.

Tell your doctor at once if you become pregnant, think you might be pregnant or are planning to become pregnant. Your doctor will urgently review your treatment.
If you are a parent or a caregiver of a female child treated with valproate, as in VELPALEX IV, you should contact their doctor once your child experiences their first period.

Important advice for male patients able to father a child
Potential risk related to taking VELPALEX IV in the 3 months prior to contraception.
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, about 5 in 100 children had such disorders when born from fathers treated with valproate, as in VELPALEX IV, and about 3 in 100 children 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 VELPALEX IV
- the need to use effective contraception (birth control) for you and your female partner during the treatment and for 3 months after stopping VELPALEX IV
- 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 VELPALEX IV use.

Breastfeeding
Sodium valproate, the active substance of VELPALEX IV, gets into the breast milk. You should not breastfeed your baby if you are receiving VELPALEX IV.

Fertility
VELPALEX IV may decrease your fertility. It is unclear if this effect is reversible after discontinuation of VELPALEX IV.
Male fertility: Using VELPALEX IV can be a contributing factor in male infertility.

Driving and using machines
You may experience drowsiness when you are first given VELPALEX IV, or if you are also taking other medicines, such as other antiepileptic medicines or benzodiazepines. If affected, you should not drive or operate machinery.
It is not always possible to predict to what extent VELPALEX IV may interfere with your daily activities. You should ensure that you do not engage in driving or operating machinery until you are aware of the measure to which VELPALEX IV affects you.

VELPALEX IV contains sodium
Velpalex contains sodium (the main component of cooking/table salt).
Each 3 mL ampoule contains 44,5 mg sodium. This is equivalent to 2 % of the recommended maximum daily dietary intake of 2 g sodium for an adult.
Each 4 mL ampoule contains 59,2 mg sodium. This is equivalent to 3 % of the recommended maximum daily dietary intake of 2 g sodium for an adult.
Each 10 mL ampoule contains 148,2 mg sodium. This is equivalent to 7 % of the recommended maximum daily dietary intake of 2 g sodium for an adult.

3. How VELPALEX IV will be administered

You will not be expected to give yourself VELPALEX IV. It will be given to you by a person who is qualified to do so.
VELPALEX IV treatment must be started and supervised by a doctor specialised in the treatment of epilepsy.

Dosage
Your doctor will decide on the amount of VELPALEX IV 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. Your doctor will tell you when you are ready to switch over to an oral dosage form of valproate.
If you have been receiving other medicines for epilepsy the dose of VELPALEX IV will be increased gradually over about 2 weeks. The total 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).

Patients with kidney problems
Your doctor may decide to adjust your or your child's dose.

Patients taking other medicines for fits (epilepsy)
You or your child may be being treated for epilepsy at the same time as VELPALEX IV. If so, your doctor should gradually initiate treatment depending on your or your child's condition.
If you have any concerns tell your doctor or nurse. It is important for you to keep having your VELPALEX IV 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. VELPALEX IV 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 receive more VELPALEX IV than you should
Since a healthcare provider will administer VELPALEX IV, he/she will control the dosage. However, in the event of concern you should contact your doctor immediately.

If you miss a dose of VELPALEX IV
Since a healthcare provider will administer VELPALEX IV, it is unlikely that the dose will be missed.

4. Possible side effects

VELPALEX IV can have side effects.
Not all side effects reported for VELPALEX IV are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using VELPALEX IV, please consult your doctor or healthcare provider for advice.

If any of the following happens, tell your doctor immediately:
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 and systems (DRESS syndrome).
liver problems and problems of the pancreas:
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.
These are all very serious side effects. If you have them, you may have had a serious reaction to VELPALEX IV. You may need urgent medical attention or further hospitalisation.

Tell your doctor immediately if you notice any of the following:
- you have a skin rash or skin lesions with a pink/red ring and a pale centre which may be fitchy, 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 allergic reaction 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 (panacytopenia) 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, or 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)
- 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 starting dose of VELPALEX IV is high or has been suddenly increased
- an increase in the number and severity of convulsions
- changes in the amount of ammonia in the blood. Symptoms of this condition are being sick, problems with balance and coordination, 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.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- anaemia (the number of red blood cells in your body is too low), causing weakness, fatigue, pale skin
- too low blood sodium concentration (signs may be mental changes, headache, nausea, vomiting, tiredness, muscle spasms)
- weight gain (see Warnings and precautions)
- state of confusion, hallucinations (seeing and hearing things that do not exist)
- aggression, agitation
- attention disturbances
- sleepiness
- convulsions
- trembling of hands and arms, clumsiness or unsteadiness
- headache
- involuntary eye movements (nystagmus)
- dizziness
- hearing loss (which may be irreversible)
- diarrhoea
- nausea, vomiting
- indigestion
- gum disease (swollen gums)
- stomach or abdominal pain
- sore mouth
- hair loss or thinning of hair
- nail and nail bed disorders
- losing bladder control (incontinence)
- painful menstrual periods.

Less frequent side effects:
- hyperandrogenism (excessive presence of male hormones in females including symptoms like excessive hair growth, acne, male pattern hair loss)
- double vision (diplopia)
- encephalopathy (an altered mental state – declining ability to reason and concentrate, memory loss, personality change, seizures and twitching may be experienced)
- lethargy (a lack of energy)
- parkinsonism (which is reversible), lack of muscle control, affected movement and speech (ataxia)
- pins and needles sensation in arms, hands, legs and feet (paraesthesia)
- dementia (which is reversible)
- trouble understanding things (cognitive disorder)
- sedation
- vasculitis (inflammation of the blood vessels – you may experience fever, fatigue, weight loss and muscle and joint pain)
- build-up of fluid in the area between the layers of tissue that line the lungs causing chest pain, cough, difficulty breathing
- skin rash
- change in hair texture, colour, growth
- decreased bone mineral density (brittle bones and fractures)
- osteoporosis (brittle bones), osteopenia (reduced bone mass)
- frequent urination at night
- inflammation of the kidneys (back pain, fever)
- fanconi syndrome: a rare disorder of kidney tubule function that causes increased urination, increased thirst, pain and weakness in muscle and bones
- absent menstrual periods or abnormal bleeding from uterus
- male infertility
- polycystic ovaries (symptoms may be weight gain, irregular periods, heavy bleeding)
- swollen breasts in males
- feeling very cold, shivering (hypothermia)
- swelling of the hands, ankles and feet
- myelodysplastic syndrome (symptoms may include fatigue, shortness of breath and unusual paleness). This is a condition where immature blood cells in the bone marrow do not mature and therefore do not become healthy blood cells.

Frequency unknown:
- malformation of the foetus and developmental disorders (see Pregnancy, breastfeeding and fertility and Warnings and precautions).

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

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of VELPALEX IV. You can also send an email directly to the safety mailbox pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store VELPALEX IV

Store all medicines out of reach of children.
Store at or below 25 °C. Do not freeze.
Keep ampoules in their original package until required for use.
The contents of the ampoule are for single use only.
Do not use VELPALEX IV after the expiry date on the label or carton.
Return any expired or unused medicine to your pharmacist for safe disposal. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Content of the pack and other information

What VELPALEX IV contains
The active substance is sodium valproate 100 mg per mL.
Each 3 mL ampoule contains sodium valproate 300 mg.
Each 4 mL ampoule contains sodium valproate 400 mg.
Each 10 mL ampoule contains sodium valproate 1 000 mg.

The other ingredients are potassium dihydrogen phosphate (buffer), disodium phosphate dodecahydrate (buffer) and water for injection.

What VELPALEX IV looks like and contents of the pack
VELPALEX IV solution for infusion or injection is a clear solution, free from visible particles.
The clear solution for injection or infusion is packed in type I transparent glass ampoules in a carton containing 1, 4, 5 or 10 ampoules:
VELPALEX 300 mg IV: 3 mL of solution is packed in a 5 mL capacity ampoule.
VELPALEX 400 mg IV: 4 mL of solution is packed in a 5 mL capacity ampoule.
VELPALEX 1 g: 10 mL of solution is packed in a 10 mL capacity ampoule.
Not all pack sizes and strengths may be marketed at one time.

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VELPALEX 300 mg IV: A53/2.5/0664
VELPALEX 400 mg IV: A53/2.5/0665
VELPALEX 1 g IV: A53/2.5/0666

Marketed by:
AFT Pharmaceuticals SA (Pty) Ltd

85847

pharma dynamics

PASIËNTINLIGTINGSBLAD

Valproaat, soos in VELPALEX® IV, kan geboortedefekte en vroeë ontwikkelingsprobleme veroorsaak indien dit tydens swangerskap toegedien word. Indien jy 'n vrou is wat swanger kan raak, moet jy vir die duur van jou behandeling effektiewe voorbehoeding gebruik (sien Swangerskap, borsvoeding en vrugbaarheid). Lig jou dokter dadelik in as jy wil swanger raak, of dink jy is dalk swanger. Indien jy die ouer of versorger is van 'n vrouelike kind wat met VELPALEX IV behandel word, lees die afdeling in hierdie inligtingsblad oor swangerskap, borsvoeding en vrugbaarheid sorgvuldig.

SKEDULERINGSTATUS: S3

VELPALEX® 300 mg IV
VELPALEX® 400 mg IV
VELPALEX® 1 g IV
Oplossing vir infusie of inspuiting (100 mg/mL)
Natriumvalproaat
Suikervry
Bevat natrium: 44,5 mg/3 mL; 59,2 mg/4 mL and 148,2 mg/10 mL

Lees die hele inligtingsblad aandagtig deur voordat VELPALEX IV aan jou gegee word
- Hou hierdie inligtingsblad. Dit mag wees dat jy dit weer moet lees.
- Indien jy nog vrae het, vra jou dokter, apteker, verpleegster of ander gesondheidsorgverskaffer.

Wat is in hierdie inligtingsblad
1. Wat is VELPALEX IV en waarvoor word dit gebruik
2. Wat jy moet weet voordat VELPALEX IV aan jou gegee word
3. Hoe VELPALEX IV toegedien sal word
4. Moontlike newe-effekte
5. Hoe VELPALEX IV bewaar sal word
6. Inhoud van die pakkie en ander inligting

1. Wat is VELPALEX IV en waarvoor word dit gebruik

VELPALEX IV bevat natriumvalproaat, wat behoort tot 'n groep medisyne genaamd anti-epileptika. Hierdie middels word gebruik om epileptiese aanvalle te beheer. VELPALEX IV oplossing vir inspuiting word gebruik om verskeie tipes epileptiese aanvalle (toevalle) te behandel wanneer natriumvalproaat tablette nie gemeen kan word nie.
VELPALEX IV word ook vir manie gebruik. Jy kan dalk opgewonde, uitbundig, rusteloos, entoesiasties of hiperaktief voel. Manie kom voor by 'n siekte genaamd "bipolêre versteuring".

2. Wat jy moet weet voordat VELPALEX IV aan jou gegee word

VELPALEX IV moet nie aan u of u kind toegedien word indien u:
- hipersensitief (allergies) is vir natriumvalproaat of enige van die bestanddele van VELPALEX IV (gelys in afdeling 6)
- lewerprobleme het, of 'n familiegeskiedenis van lewerprobleme
- aan porfirie ly ('n seldsame toestand wat die afbraak van komponente van rooibloedselle beïnvloed)
- 'n genetiese probleem het wat 'n mitochondriale versteuring veroorsaak (bv. Alpers-Huttenlocher-sindroom)
- aan ureumsiklusversteuring ('n tipe metaboliese versteuring) ly
- swanger is, of daar 'n moontlikheid bestaan dat u swanger mag raak:
  - vir die behandeling van epilepsie:
    - indien u, of u vrouelike (meisie) kind swanger is, tensy daar geen alternatiewe, doeltreffende behandeling beskikbaar is nie (kyk Swangerskap, borsvoeding en fertiliteit: Swangerskap – Belangrike inligting vir vrouens)
    - indien dit moontlik is dat u, of u vrouelike (meisie) kind, swanger kan raak, tensy voorwaardes van die Swangerskapvoorkomingsprogram nagekom word (kyk Swangerskap, borsvoeding en fertiliteit: Swangerskap – Belangrike inligting vir vrouens
  - vir die behandeling van bipolêre versteuring:
    - indien u swanger is
    - indien u 'n vrou is wat moontlik swanger kan raak, tensy die voorwaardes van die swangerskapvoorkomingsprogram nagekom word (kyk Swangerskap – Belangrike inligting vir vrouens)
- 'n aangebore karnitien tekort ('n baie seldsame metaboliese siekte) het, wat nie behandel word nie.

Waarskuwings en voorsorgmaatreëls
Praat met jou dokter of gesondheidsorgverskaffer voordat jy VELPALEX IV ontvang, indien jy:
- diabetes het. VELPALEX IV kan die resultate van urinetoetse beïnvloed
- 'n karnitien-palmitoïeltransferase tipe II-tekort het, wat verhoed dat die liggaam sekere vette vir energie gebruik, aangesien jy meer geneig kan wees tot ernstige newe-effekte
- nierprobleme het. Jou dokter kan moontlik 'n laer dosis vir jou voorskryf
- 'n breinsiekte het of 'n metaboliese siekteboestand wat jou brein aantas
- 'n 'ureumsiklusversteuring' het, waarby te veel ammoniak in die liggaam opbou
- 'n siekte genaamd 'sistemiese lupus eritematose' (SLE) het – 'n siekte van die immuunstelsel wat die vel, bene, gewrigte en inwendige organe aantas
- weet dat daar 'n genetiese probleem is wat veroorsaak word deur 'n mitochondriale versteuring in jou familie. Indien jy nie seker is of enige van die bogenoemde op jou van toepassing is nie, praat met jou dokter of apteker voordat jy VELPALEX IV ontvang
- 'n operasie ondergaan, insluitend tandheelkundige chirurgie, lig die dokter of tandarts in dat jy VELPALEX IV ontvang. Jy moet ekstra sorg neem om jou tande skoon te borsel om infeksie te voorkom, aangesien newe-effekte van VELPALEX IV bloeding en swelling van die tandvleis insluit (sien afdeling 4).

Leverskade
VELPALEX IV kan ernstige en lewensgevaarlike skade aan jou lever veroorsaak. Tekens wat jy dalk kan opmerk, sluit in aanvalle wat ernstiger word of meer gereeld voorkom, of uitermatige moegheid, gebrek aan energie, swakheid, maagpyn, verlies van eetlus, naarheid, braking, geel vel en oogwitte of swelling van die gesig. Lig dadelik jou dokter in as jy enige van hierdie simptome waarneem. Die risiko vir leverskade neem toe, indien u kind jonger as 3 jaar oud is, en ander anti-epileptiese medisyne saam met VELPALEX IV neem, of ander neurologiese of metaboliese siekites en erger vorms van epilepsie het.
As u kind jonger as 3 jaar is, moet VELPALEX IV nie saam met aspirien toegedien word nie.

Skade aan die pankreas
VELPALEX IV kan ernstige of lewensgevaarlike skade aan die pankreas veroorsaak. Dit kan enige tyd tydens jou behandeling voorkom. Indien jy enige van die volgende simptome ervaar, lig jou dokter dadelik in: maagpyn, naarheid, braking of verlies van eetlus.

Selfdood-gedagtes en -gedrag
'n Klein groepie mense wat met anti-epileptika soos natriumvalproaat behandel word, het gedagtes van self-besering of selfdood gehad. Indien jy op enige tydstip sulke gedagtes koester, moet jy dadelik jou dokter kontak.
Daar kan ook 'n risiko wees dat jy verandertinge in jou geestesgesondheid sal ervaar as jou siektetoestand nie behandel word nie.

Stuipbrekings
Stuipbrekings kan erger word of meer dikwels voorkom terwyl hierdie medisyne gebruik word. Indien dit gebeur kontak dadelik jou dokter.

Gewigstoename
Gebruik van VELPALEX IV kan jou laat gewig aansit. Gesels met jou dokter oor hoe dit jou sal beïnvloed.

Bloedtoetse
Jou dokter sal dalk bloedtoetse wil doen voordat VELPALEX IV aan jou gegee word en tydens jou behandeling.

Karnitien-palmitoïeltransferase tipe II tekort
Indien u, of u kind ingelig is dat u karnitien-palmitoïeltransferase tipe II tekort het.

Bipolêre versteuring
VELPALEX IV moet nie gebruik word vir die behandeling van manie, wat verband hou met bipolêre versteurings by kinders en adolessente jonger as 18 jaar nie.

Kinders en adolessente
Gedurende behandeling met VELPALEX IV moet kinders onder 3 jaar nie salisilate (aspirien) gegee word nie, weens die risiko van levertoksisiteit. Daarbenewens moet jy nie salisilate by kinders jonger as 16 jaar gebruik nie, aangesien dit die risiko van Reye-sindroom ('n akute toestand wat swelling in die brein en lever veroorsaak) kan verhoog.

Kinders (mantlik en vrouelik) onder 18 jarige ouderdom:
VELPALEX IV moet met omsigtigheid gebruik word vir die behandeling van epilepsie by mantlike en vrouelike kinders jonger as 18 jaar.
Maak seker dat die voorwaardes van die swangerskapvoorkomingsprogram nagekom word vir vrouelike kinders.
Sommige psigiatriese versteurings, insluitend aggressie, agitasie, aandagversteuring, abnormale gedrag, psigomotoriese hiperaktiwiteit en leerprobleme kan by pediatriese pasiënte wat VELPALEX IV ontvang waargeneem word (sien Moontlike newe-effekte). Daar is tans geen afdoende bewyse rakende die moontlikheid van skade aan die voortplantingstelsel, skeletstelselgroei of breinontwikkeling by pasiënte onder die ouderdom van 18 jaar nie.

Ander medisyne en VELPALEX IV
Lig altyd jou gesondheidsorgverskaffer in as jy enige ander medisyne neem. Dit sluit komplementêre of tradisionele medisyne in.

Die volgende medisyne kan die kans verhoog dat jy newe-effekte kry wanneer dit saam met VELPALEX IV gegeef word:
- sommige medisyne wat gebruik word om pyn en inflammasie (salisilate) soos aspirien
- sommige ander medisyne wat gebruik word om aanvalle te behandel – sien afdeling 3. Pasiënte wat ander medisyne neem vir toevalle (epilepsie). Dit sluit medisyne in soos fenobarbitaal, primidone, fenitoïen, karbamasepien, rufinamied, topiramaat, lamotrigien en felbamaat
- asetasolamiedgebruik vir die behandeling van glukoom, edemo of toevalle. Die kombinasie saam met VELPALEX IV mag ammoniak in die liggaam laat opbou.

VELPALEX IV inspuiting kan die effek van die volgende medisyne verster:
- medisyne vir depresie, byvoorbeeld monoamenioksidase-inhibeerders (MAOI) soos moklobemied, selegiline
- medisyne wat gebruik word om emosionele en geestesgesondheidsprobleme te verlig (insluitend skizofrenie, bipolêre versteuring en depressie) soos kwetiapien, olanzapien, olanzapien en litium
- propofol – gebruik vir narkose
- sidovudien – gebruik vir die behandeling van MIV-infeksie
- nimodipien (gebruik om probleme as gevolg van 'n sekere tipe bloeding in die brein te verminder)
- temozolomiedgebruik vir die behandeling van kanker
- medisyne gebruik om die bloed te verdun (soos warfarien).

Die volgende medisyne kan die manier waarop VELPALEX IV werk beïnvloed:
- sommige medisyne wat gebruik word vir die voorkoming en behandeling van malaria, soos mefloksien en chloroksien
- simetidien, gebruik vir maagsere
- antibiotika bv. ertromisien, karbapenems (antibiotika gebruik vir die behandeling van bakteriële infeksies). Die kombinasie van valproïensuur en karbapenems moet vermy word omdat dit die effek van natriumvalproaat kan verminder
- rifampisien, gebruik vir die behandeling van tuberkulose en ander infeksies
- proteaseremmers soos lopinavir en ritonavir – gebruik vir MIV-infeksie en VIGS
- cholestiramien, gebruik om bloedvetvlakke (cholesterol) te verlaag. Jy kan egter steeds VELPALEX IV kry; jou dokter sal jou raad gee oor wat geskik is vir jou
- estrogeen-bevattende produkte (insluitend sommige voorbehoedpille)
- metamisool, 'n pynstiller, wat die effek van VELPALEX IV kan verminder
- metotreksaat (gebruik vir kanker en inflammatoriese siektes) kan verminder word
- sommige anti-infektiewe middels, wat pivalaat bevat (pivampisillien, adefovirdipivoksil)
- kannabidiol (algemeen bekend as CBD en gebruik word vir epilepsie en ander toestande).

Gebruik van VELPALEX IV met kos en drinkgoed
Die inname van alkoholiese drankies tee die behandeling word nie aanbeveel nie.
Jy moet nie alkoholiese drankies neem terwyl jy met VELPALEX IV behandel word nie.

Swangerskap, borsvoeding en vrugbaarheid

Indien jy swanger is of bevoorsk word, dink jy is dalk swanger, of beplan om 'n baba te hê, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgverskaffer voordat hierdie medisyne aan jou toegedien word.

Swangerskap

As jy swanger is moet VELPALEX IV nie aan jou gegee word nie, tensy ander behandelings nie effektief is of goed verdra word nie.
Moenie ophou om VELPALEX IV te ontvang sonder om jou dokter te raadpleeg nie, aangesien dit skade aan jou of 'n ongebore kind kan veroorsaak.
As jy 'n vrou is wat 'n baba kan hê, moet jy nie VELPALEX IV ontvang nie, tenzy jy 'n effektiewe metode van voorbehoeding (kontrasepsie) tydens jou behandeling met VELPALEX IV gebruik. Praat met jou dokter as jy enige vrae het oor watter voorbehoedmetode geskik is vir jou.
VELPALEX IV kan wanneer dit aan vrouelike swangerpasiënte by kinders wat in die baarmoeder aan valproaat blootgestel word veroorsaak.

VELPALEX IV kan ernstige geboortedefekte veroorsaak en kan die ontwikkeling van die kind tydens die groeiprosess beïnvloed. Geboortedefekte wat aangemeld is, sluit in spina bifida (waar die bene van die ruggraat nie behoorlik ontwikkel is nie); gesig- en skedelmisvormings; misvormings van die hart, niere, urineweg en geslagsdele; gebrekkige ledemate.
Gehoorprobleme of doofheid is aangemeld by kinders wat tydens swangerskap aan valproaat blootgestel is.

Daar word beraam dat tot 30 - 40 % van voorskoolse kinders wie se moeders natriumvalproaat tydens swangerskap geneem het, probleme met vroeë kinderontwikkeling kan hê. Kinders wat geaffiseerd word kan stadiger loop en praat, is intellektueel tot minder in staat as ander kinders, en suikkel meer taal en gehoue. Outistiese spektrum afwykings word meer gereld gediagnoseer by kinders wat blootgestel is aan valproaat tydens swangerskap. Indien jy 'n bewyse dat kinders wat tydens swangerskap aan natriumvalproaat blootgestel was, 'n groter risiko het om aandaggebrek-hiperaktiwiteitsteuring (ADHS) te ontwikkel.

Voordat hierdie medisyne aan jou voorgeskryf word, sou jou dokter verduidelik het wat met jou baba kan gebeur as jy swanger word terwyl jy VELPALEX IV ontvang. Indien jy later besluit om 'n kind te hê, moet jy nie ophou om jou medisyne of metode van gebo