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(*Ministry of Health Malaysia*)
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Tarikh : 18 Ogos 2025

SEMUA PEMEGANG PENDAFTARAN PRODUK

SEMUA PERSATUAN BERKENAAN
(SEPERTI DI SENARAI EDARAN)

Tuan / Puan,

PERATURAN-PERATURAN KAWALAN DADAH DAN KOSMETIK 1984
ARAHAN PENGARAH PERKHIDMATAN FARMASI BILANGAN 15 TAHUN 2025 DIREKTIF UNTUK SEMUA PRODUK YANG MENGANDUNGI VALPROATE TERMASUK TERBITANNYA (SODIUM VALPROATE, VALPROIC ACID) :

i. **PENGEMASKINIAN SISIP BUNGKUSAN DAN RISALAH MAKLUMAT UBAT UNTUK PENGGUNA (RiMUP) DENGAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO *NEURODEVELOPMENTAL DISORDER* (NDD), TRANSGENERASI DAN KETIDAKSUBURAN PADA LELAKI (*MALE INFERTILITY*)**

ii. **PENYEDIAAN BAHAN-BAHAN PENGAJARAN *(EDUCATIONAL MATERIALS)* BAGI RISIKO *NEURODEVELOPMENTAL DISORDER* (NDD)**

Dengan hormatnya saya merujuk kepada perkara di atas.

2. Dikemukakan Arahan Pengarah Perkhidmatan Farmasi Bilangan 15 Tahun 2025 untuk makluman dan perhatian semua Pemegang Pendaftaran Produk (PRH). Tuan / Puan adalah diarahkan untuk mematuhi keperluan tersebut.

Sekian, terima kasih.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah,

(ROSLIZA BINTI LAJIS) RPh.3376
Timbalan Pengarah
b.p. Pengarah Bahagian Regulatori Farmasi Negara
Kementerian Kesihatan Malaysia

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ARAHAN DI BAWAH PERATURAN 29 PERATURAN – PERATURAN KAWALAN DADAH DAN KOSMETIK 1984

BILANGAN 15 TAHUN 2025

DIREKTIF UNTUK SEMUA PRODUK YANG MENGANDUNGI VALPROATE TERMASUK TERBITANNYA (SODIUM VALPROATE, VALPROIC ACID):

i. **PENGEMASKINIAN SISIP BUNGKUSAN DAN RISALAH MAKLUMAT UBAT UNTUK PENGGUNA (RiMUP) DENGAN MAKLUMAT KESELAMATAN BERKAITAN RISIKO *NEURODEVELOPMENTAL DISORDER* (NDD), TRANSGENERASI DAN KETIDAKSUBURAN PADA LELAKI (*MALE INFERTILITY*)**

ii. **PENYEDIAAN BAHAN-BAHAN PENGAJARAN *(EDUCATIONAL MATERIALS)* BAGI RISIKO *NEURODEVELOPMENTAL DISORDER* (NDD)**

1. TUJUAN

1.1 Jawatankuasa Penasihat Kesan Advers Ubat Kebangsaan (MADRAC) dalam mesyuarat kali ke-194 pada 26 Jun 2025 telah mencadangkan pengemaskinian sisip bungkusan dan Risalah Maklumat Ubat untuk Pengguna (RiMUP) bagi semua produk yang mengandungi valproate termasuk terbitannya (sodium valproate, valproic acid) dengan maklumat keselamatan berkaitan risiko *neurodevelopmental disorder* (NDD), risiko transgenerasi dan ketidaksuburan pada lelaki *(male infertility)* termasuk menyediakan bahan-bahan pengajaran (*educational materials*) bagi menerangkan risiko NDD.

1.2 Di bawah peruntukan Peraturan 8, Peraturan-Peraturan Kawalan Dadah dan Kosmetik 1984 (PKDK 1984), Pihak Berkuasa Kawalan Dadah (PBKD) dalam mesyuarat kali ke-**411** pada **7 Ogos 2025** telah membuat keputusan berkenaan perkara tersebut di atas.

1.3 Sehubungan dengan itu, arahan ini dikeluarkan oleh Pengarah Perkhidmatan Farmasi di bawah peruntukan Peraturan 29, PKDK 1984 untuk memaklumkan Pemegang Pendaftaran Produk (PRH) berhubung perkara ini.

2. PELAKSANAAN

2.1 Pengemaskinian ke atas sisip bungkusan dan Risalah Maklumat Ubat untuk Pengguna (RiMUP) bagi semua produk yang mengandungi valproate termasuk terbitannya adalah seperti berikut:

2.1.1 Sisip bungkusan

(a) Pada bahagian *Warnings & Precautions:*

Use in male patients of reproductive potential

A retrospective observational study indicates an increased risk of neurodevelopmental disorders (NDDs) in children born to men treated with valproate in the 3 months prior to conception, compared to those treated with lamotrigine or levetiracetam (see Pregnancy). Despite study limitations, by way of precautions, the prescriber should inform the male patients of this potential risk. The prescribers should discuss with the patient, the need for effective contraception, including for the female partner, while using valproate and for 3 months after stopping the treatment. The risk to children born to men stopping valproate at least 3 months prior to conception (i.e., allowing a new spermatogenesis without valproate exposure) is not known.

The male patient should be advised:

- *not to donate sperm during treatment and for 3 months after stopping the treatment,*

- *of the need to consult his doctor to discuss alternative treatment options, as soon as he is planning to father a child, and before discontinuing contraception,*
- *that he and his female partner should contact their doctor for counseling in case of pregnancy if he used valproate within 3 months prior to conception.*

The male patient should also be informed about the need for regular (at least annual) review of treatment by a specialist experienced in the management of epilepsy or bipolar disorder. The specialist should at least annually review whether valproate is the most suitable treatment for the patient. During this review, the specialist should ensure the male patient has acknowledged the risk and understood the precautions needed with valproate use (Annual Risk Acknowledgement Form). Educational materials are available for healthcare professionals and male patients. A patient guide should be provided to all men of reproductive potential using valproate

(b) Pada bahagian *Reproduction:*

<u>Teratogenicity and developmental effects from female and male exposure</u>

Risk to children of fathers treated with valproate

A retrospective observational study on electronic medical records in 3 European Nordic countries indicates an increased risk of neuro-developmental disorders (NDDs) in children (from 0 to 11 years old) born to men treated with valproate in the 3 months prior to conception, compared to those treated with lamotrigine or levetiracetam. The adjusted cumulative risk of NDDs ranged between 4.0% to 5.6% in the valproate group versus between 2.3% to 3.2% in the composite lamotrigine/levetiracetam monotherapy group. The pooled adjusted hazard ratio (HR) for NDDs overall obtained from the meta-analysis of the datasets was 1.50 (95% CI: 1.09-2.07).

Due to study limitations, it is not possible to determine which of the studied NDD subtypes (autism spectrum disorder, intellectual disability, communication disorder, attention deficit/hyperactivity disorder, movement disorders) contributes to the overall increased risk of NDDs. Alternative therapeutic options and the need for effective contraception while using valproate and for 3 months after stopping the treatment should be discussed with male patients of reproductive potential, at least annually (see Warnings/Precautions)

Fertility
Valproate administration may also impair fertility in men (see Section Adverse Reactions). In the few cases in which valproate was switched/discontinued or the daily dose reduced, the decrease in male fertility potential was reported as reversible in most but not all cases, and successful conceptions have also been observed.

(c) Pada bahagian *Adverse Effects/ Undesirable Effects:*

Reproductive system and breast disorders:
Rare: male infertility

(d) Pada bahagian *Nonclinical Safety Data:*

Reproductive and developmental toxicity

Teratogenic effects (malformations of multiple organ systems) have been demonstrated in mice, rats, and rabbits.

In published literature, behavioural abnormalities have been reported in first generation offspring of mice and rats after in utero exposure to clinically relevant doses/exposures of valproate. In mice, behavioural changes have also been observed in the 2nd and 3rd generations, albeit less pronounced in the 3rd generation, following an acute in utero exposure of the first generation. The relevance of these findings for humans is unknown.

Impairment of fertility

In sub-chronic/ chronic toxicity studies, testicular degeneration/atrophy or spermatogenesis abnormalities and a decrease in testes weight were reported in adult rats and dogs after oral administration starting at doses of 400 mg/kg/day and 150 mg/kg/day, respectively with associated NOAELs for testis findings of 270 mg/kg/day in adult rats and 90 mg/kg/day in adult dogs. In a fertility study in rats, valproate at doses up to 350 mg/kg/day did not alter male reproductive performance.

In juvenile rats, a decrease in testes weight was only observed at doses exceeding the maximum tolerated dose (from 240 mg/kg/day by intraperitoneal or intravenous route) and with no associated histopathological changes. No effects on the male reproductive organs were noted at tolerated doses (up to 90 mg/kg/day). Relevance of the testicular findings to pediatric population is unknown.

2.1.2 Risalah Maklumat Ubat untuk Pengguna (RiMUP)

(a) Pada bahagian *While you are using it:*

Important advice for male patients able to father a child

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

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

As a precautionary measure, your doctor will discuss with you

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

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

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

(b) Pada bahagian *Side effects:*

- male infertility (may be reversible after dose reduction or discontinuation)

2.2 Penyediaan bahan-bahan pengajaran *(educational materials*) bagi valproate termasuk terbitannya sebagai panduan kepada preskriber dan pesakit lelaki (bagi risiko *neurodevelopmental disorder*). Bahan-bahan pengajaran yang perlu disediakan adalah seperti berikut:

2.2.1 Kad pesakit

(a) Boleh diedarkan semasa pesakit kali pertama menerima rawatan valproate termasuk terbitannya sebagai rujukan bersama-sama penerangan yang jelas berkaitan risiko ini.

(b) Maklumat ringkas yang perlu dimasukkan dalam kad pesakit bagi pesakit lelaki adalah seperti berikut:

Males (of reproductive potential) using valproate:

- There is a possible risk of movement and mental developmental disorders in children when valproate is taken by male patients in the 3 months before conception.
- Discuss this possible risk and the need for effective contraception with your doctor.
- Valproate is an effective medicine for epilepsy and bipolar disorder.
- Never stop taking valproate unless your doctor tells you to as your condition may become worse.
- If you are planning for a child, do not stop using valproate and contraception before you speak to your doctor.
- Ask your doctor for the patient guide.

2.2.2 Borang senarai semak pesakit untuk kegunaan preskriber (*annual risk acknowledgement form)* (rujuk Lampiran 1)

(a) Borang ini diguna pakai semasa:

i. pesakit kali pertama dipreskrib valproate termasuk terbitannya

ii. penilaian pada setiap tahun rawatan

(b) Borang ini bertujuan untuk memastikan preskriber telah memaklumkan dan berbincang dengan pesakit atau penjaganya berkaitan rawatan ubat yang mengandungi valproate termasuk terbitannya dan risiko berkaitan. Preskriber juga perlu memastikan pesakit memahami maklumat yang telah disampaikan.

(c) Bahagian A dan B pada borang perlu dilengkapkan dan ditandatangani oleh preskriber. Bahagian B pada borang perlu ditandatangani juga oleh pesakit/penjaga.

(d) Satu (1) salinan borang (bahagian A dan B) perlu disimpan untuk rujukan preskriber dan satu (1) salinan bahagian B diberikan untuk simpanan pesakit/penjaga.

2.2.3 Risalah panduan bagi profesional kesihatan dan pesakit (rujuk Lampiran 2 dan 3)

(a) Risalah panduan ini bertujuan untuk memberi maklumat kepada profesional kesihatan sebagai panduan perawatan dan kepada pesakit bagi memberikan maklumat berkaitan langkah-langkah yang perlu diambil bagi mengurangkan risiko susulan penggunaan valproate termasuk terbitannya.

(b) Risalah panduan bagi pesakit boleh diedarkan oleh profesional kesihatan seperti pegawai perubatan dan pegawai farmasi semasa pesakit menerima rawatan valproate termasuk terbitannya, contohnya semasa temujanji rawatan atau semasa pendispensan ubat.

2.2.4 Maklumat umum berkaitan penyediaan bahan – bahan pengajaran kepada preskriber dan juga pesakit lelaki mengenai risiko terbaharu ini:

(a) Borang senarai semak pesakit untuk kegunaan preskriber (*annual risk acknowledgement form*) ini perlu dicetak kerana ianya memerlukan tandatangan preskriber dan pesakit. Ia perlu dibekalkan oleh syarikat Pemegang Pendaftaran Produk (PRH) untuk edaran ke fasiliti-fasiliti yang dibekalkan dengan valproate termasuk terbitannya.

(b) Kad pesakit juga perlu dicetak dan dibekalkan oleh syarikat PRH untuk edaran ke fasiliti-fasiliti yang dibekalkan dengan valproate dan terbitannya.

(c) Untuk Risalah Panduan bagi profesional kesihatan dan pesakit, syarikat PRH mempunyai pilihan untuk mengedarkannya dalam bentuk cetakan atau melalui kod QR.

(d) Sekiranya pihak syarikat PRH memilih untuk mengedarkannya melalui kod QR, ianya boleh dilaksanakan seperti berikut :

i. Untuk edaran kepada preskriber: kod tersebut perlu diletakkan pada borang senarai semak pesakit untuk kegunaan preskriber *(annual risk acknowledgement form)* yang dicetak.

ii. Untuk edaran kepada pesakit : kod tersebut perlu diletakkan pada kad pesakit yang dicetak.

2.3 Tarikh pelaksanaan keperluan mengemas kini maklumat berkenaan pada semua produk yang mengandungi valproate termasuk terbitannya adalah seperti berikut :

(a) Permohonan baharu dan produk yang sedang dalam proses penilaian : **1 September 2025**

(b) Produk berdaftar : **1 Mac 2026**

2.4 Permohonan pindaan pada sisip bungkusan dan RiMUP bagi produk berdaftar perlu dikemukakan sebagai permohonan variasi *MiV PA2 - Change of product labeling (in accordance to country specific labeling requirement).*

3. TARIKH KUAT KUASA

3.1 Tarikh kuat kuasa arahan ini ialah mulai **1 September 2025.**

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

(DR. AZUANA BINTI RAMLI) RPh.1889
Pengarah Perkhidmatan Farmasi
Kementerian Kesihatan Malaysia
sab/nlaj/pkpsr/npra

s.k.

1. Timbalan Ketua Pengarah Kesihatan (Kesihatan Awam), Kementerian Kesihatan Malaysia (KKM)
2. Timbalan Ketua Pengarah Kesihatan (Perubatan), KKM
3. Pengarah Bahagian Regulatori Farmasi Negara, KKM
4. Pengarah Bahagian Amalan dan Perkembangan Farmasi, KKM
5. Pengarah Bahagian Penguatkuasaan Farmasi, KKM
6. Pengarah Bahagian Dasar dan Perancangan Strategik Farmasi, KKM

LAMPIRAN 1

BORANG SENARAI SEMAK PESAKIT UNTUK KEGUNAAN PRESKRIBER
(*ANNUAL RISK ACKNOWLEDGEMENT FORM)*

Annual Risk Acknowledgment Form for male patients of reproductive potential treated with valproate (*Product Name*)

Read, complete and sign this form during a visit with the specialist: at treatment initiation and at the annual visit. This is to make sure that after discussion with their specialist, male patients or their caregiver acknowledged the potential risk and understood the precautions associated with valproate use.

Part A. To be completed and signed by the Specialist

Name of patient or caregiver: _____

I have discussed the following information with the above-named patient or caregiver:

The potential risk of neurodevelopmental disorders (NDDs) in children born to males treated with valproate in the 3 months prior to conception: • A retrospective observational study on electronic medical records in 3 European Nordic countries indicates an increased risk of neuro-developmental disorders (NDDs) in children (from 0 to 11 years old) born to men treated with valproate in the 3 months prior to conception, compared to those treated with lamotrigine or levetiracetam. • The adjusted cumulative risk of NDDs ranged between 4.0% to 5.6% in the valproate group versus between 2.3% to 3.2% in the composite lamotrigine/levetiracetam monotherapy group. The pooled adjusted hazard ratio (HR) for NDDs overall obtained from the meta-analysis of the datasets was 1.50 (95% CI: 1.09-2.07). • Due to study limitations, it is not possible to determine which of the studied NDDs subtypes (autism spectrum disorder, intellectual disability, communication disorder, attention deficit/hyperactivity disorder, movement disorders) contributes to the overall increased risk of NDDs. • The risk to children born to men stopping valproate at least 3 months prior to conception (i.e., allowing a new spermatogenesis without valproate exposure) is not known.	☐
The need for regular (at least annual) review of the treatment and consideration of alternative therapeutic options.	☐
The need for effective contraception, including for the female partner, while using valproate and for 3 months after stopping the treatment.	☐
That the patient should not donate sperm during treatment and for 3 months after stopping the treatment.	☐
The need for patient to consult his doctor to discuss alternative treatment options as soon as he is planning to father a child, and before discontinuing contraception.	☐
The need for patient and his female partner to contact their doctor for counselling in case a child was conceived while he used valproate within 3 months prior to conception.	☐
That the patient should not stop taking valproate without talking to their doctor, as the epilepsy or bipolar disorder could become worse.	☐
I have given the patient or caregiver a copy of the patient guide.	☐

Name of Specialist Signature Date

LAMPIRAN 1

BORANG SENARAI SEMAK PESAKIT UNTUK KEGUNAAN PRESKRIBER
(*ANNUAL RISK ACKNOWLEDGEMENT FORM)*

Annual Risk Acknowledgment Form for male patients of reproductive potential treated with valproate (*Product Name*)

Read, complete and sign this form during a visit with your specialist: at treatment initiation and at the annual visit. This is to make sure that after discussion with your specialist, you or your caregiver acknowledged the potential risk and understood the precautions associated with valproate use.

Part B. To be completed and signed by the Patient or caregiver.

That I should visit a specialist regularly (at least annually) to review whether valproate treatment remains the best option for me.	☐
The potential risk of taking valproate in male patients when planning to have a child: • A study suggests that if I take valproate in the 3 months prior to conception, my child may have a higher risk for impaired mental and/or motor development compared to children born to males who used lamotrigine or levetiracetam, other medicines that can be used to treat my disease. • In this study, around 5 children in 100 had such disorders when born from male patients treated with valproate, and around 3 children in 100 from male treated with the other medicines. • There are no data on this potential risk to children of male patients conceived more than 3 months after stopping valproate treatment (the time needed for new sperm to be formed).	☐
That I and my female partner should use effective contraception (birth control) while I am treated with valproate and for 3 months after stopping treatment.	☐
That I need to consult my doctor to discuss alternative treatment options, as soon as I plan for a child, and before discontinuing contraception (birth control).	☐
That I should not donate sperm during treatment with valproate and for 3 months after stopping treatment.	☐
The need for both me and my female partner to contact the doctor for counselling in case we conceived a child while I was using valproate in the 3 months prior to conception.	☐
That I should not stop my treatment without talking to my doctor. If I stop my treatment, my symptoms may become worse.	☐
I have received a copy of the patient guide	☐

Name of patient or caregiver Signature Date

LAMPIRAN 2

GUIDE FOR HEALTHCARE PROFESSIONALS
RISK OF NEURODEVELOPMENTAL DISORDERS (NDDs) FOLLOWING USE OF SODIUM VALPROATE IN MALE PATIENTS OF REPRODUCTIVE POTENTIAL

Note: This guide is to inform you of important information and strengthened warnings related to this risk

BACKGROUND INFORMATION: SAFETY DATA

A retrospective observational study was conducted using data from multiple registry databases in Denmark, Sweden and Norway to investigate the risk of NDDs in offspring paternally exposed to valproate as monotherapy, compared to lamotrigine or levetiracetam as monotherapy treatment, in the 3 months period prior to conception. The main outcome of interest was NDDs (composite endpoint including autism spectrum disorders, intellectual disability, communication disorders, attention deficit/hyperactivity disorders, movement disorders) in offspring up to 11 years of age. The mean follow-up time of children in the valproate group ranged between 5.0 and 9.2 years compared to 4.8 and 6.6 years for children in the lamotrigine/levetiracetam group.

1. Risk of Neurodevelopmental Disorders (NDDs)

- The meta-analysis of data from the 3 countries resulted in a pooled adjusted hazard ratio (HR) of 1.50 (95% CI: 1.09-2.07) for NDDs in children from males treated with valproate monotherapy in the 3 months prior to conception compared to the composite lamotrigine/levetiracetam monotherapy group.
- The adjusted cumulative risk of NDDs ranged between 4.0% to 5.6% in the valproate group monotherapy versus between 2.3% to 3.2% in the composite lamotrigine/levetiracetam monotherapy group.
- Due to study limitations, it is not possible to determine which of the studied NDD subtypes(autism spectrum disorder, intellectual disability, communication disorder, attention deficit/hyperactivity disorder, movement disorders) contributes to the overall increased risk of NDDs.
- The risk to children born to male patients stopping valproate at least 3 months prior to conception (i.e., allowing a new spermatogenesis without valproate exposure) is not known

LAMPIRAN 2

GUIDE FOR HEALTHCARE PROFESSIONALS
RISK OF NEURODEVELOPMENTAL DISORDERS (NDDs) FOLLOWING USE OF SODIUM VALPROATE IN MALE PATIENTS OF REPRODUCTIVE POTENTIAL

Recommendations for valproate use in male patients of reproductive potential

- **The use of sodium valproate in male patients is initiated and supervised by a specialist experienced in treatment of epilepsy or bipolar disorder.**
- **Male patients should be informed about the potential risk of Neurodevelopmental Disorders (NDDs) and the need to consider effective contraception, including for a female partner, while using valproate and for 3 months after stopping the treatment;**
- **Treatment with valproate in male patients should be regularly reviewed by prescribers to evaluate whether valproate remains the most suitable treatment for the patient.**
- **For male patients planning to have a child, suitable alternative treatment options should be considered and discussed with the patient. Individual circumstances should be evaluated for each patient. It is recommended that advice from a specialist experienced in the management of epilepsy or bipolar should be sought as appropriate.**
- **The male patients should be advised to not donate sperm during treatment and for at least 3 months after treatment discontinuation.**

COUNSELLING POINT

- advise patient/ caregiver on the risk of neurodevelopmental disorders associated with children from men taking sodium valproate three (3) months prior to conception.
- advise patient and his female partner to use effective contraception without interruption throughout the entire duration of sodium valproate treatment and three (3) months after stopping the drug.
- Inform patient not to donate sperm during treatment and for three (3) months after stopping the treatment
- inform patient also about the risks of untreated seizure or bipolar disorder and advise patient not to stop treatment abruptly.
- ensure that patient/ caregiver acknowledges the potential risk and understands the precautions associated with sodium valproate using the annual risk acknowledgement form for males and receives the patient card and patient guide provided by the product registration holder of sodium valproate.

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LAMPIRAN 3

GUIDE FOR MALE PATIENTS
RISK OF NEURODEVELOPMENTAL DISORDERS (NDDs) FOLLOWING USE OF SODIUM VALPROATE IN MALE PATIENTS OF REPRODUCTIVE POTENTIAL

This guide contains key information about the potential risk of sodium valproate when used by male patients of reproductive potential in the three (3) months before conception of a child.
Ask your doctor or pharmacist if you have any questions.

INFORMATION ABOUT THE RISK:

A study suggests a possible risk of movement and mental developmental disorders (problems with early childhood development) in children born to males treated with valproate in the 3 months before conception. In this study, around 5 children in every 100 had such disorders when born to males treated with valproate, as compared to around 3 children in every 100 when born to males treated with lamotrigine or levetiracetam (other medicines that can be used to treat your disease).

However, the study has limitations and therefore it is not entirely clear if the increased risk for movement and mental developmental disorders suggested by this study is caused by valproate. A wide range of movement and mental developmental disorders were investigated in the study. However, the study was not large enough to show which particular type of disorder children may be at risk of developing. For example, problems with your child's movement and mental development as they grow up may include :

- Movement problems
- Lower intelligence than other children of the same age
- Poor speech and language skills
- Autism or autistic spectrum problems
- Attention Deficit and/or Hyperactivity Disorder

What you must do if you are being prescribed sodium valproate:

- Use **effective contraception** (birth control) for you and your female partner during valproate use and for three (3) months after stopping valproate (the time needed for new sperm to be formed).
- Consult your doctor when you **are planning to conceive a child** and before stopping contraception.
- Ask your doctor of the possibility of **other treatments** that can be used to treat your disease, depending on your individual situation.
- **Do not donate sperm** when taking valproate and for three (3) months after stopping valproate treatment.
- **Talk to your doctor** if you are planning a child.
- If your **female partner becomes pregnant** while you used valproate in the three (3) months before conception and you have questions, **contact your doctor.**
- **Do not stop your treatment** without talking to your doctor. If you stop your treatment, your symptoms may become worse.
- Follow your **regular appointments** with your prescriber.
- Discuss with your doctor if you have any concerns and report any side effects.