THIS GUIDE IS INTENDED FOR GIRLS (OF ANY AGE) AND WOMEN WHO MAY BECOME PREGNANT DURING TREATMENT WITH VALPROATE

A GUIDE ON CONTRACEPTION AND PREGNANCY FOR PATIENTS TREATED WITH VALPROATE

For full product information, read this guide together with the leaflet for the patient

VALPROATE CONTRACEPTION AND PREGNANCY: WHAT YOU NEED TO KNOW

This guide provides key information on the risks of using valproate during pregnancy.
In case of any doubt check with your doctor, midwife or pharmacist.

KEEP THIS GUIDE, SO THAT IT CAN BE REREAD IF NECESSARY.

PL.EDU.VAL.24.04.02

Information on the use of valproate in girls (of any age) and women who may become pregnant, and the risks of using valproate during pregnancy, can be also found online at www.walproiniany.pl

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MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

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1 Highlights to remember

- Valproate is an effective drug used in the treatment of epilepsy and bipolar affective disorder.
- Valproate should only be taken by women or girls (of any age) if other methods of treatments do not work. This is because valproate taken during pregnancy may seriously damage the foetus.

If the patient taking valproate is capable of becoming pregnant:
- she should always use effective contraception (birth control);
- she should not discontinue contraceptive agents at any time.

In the case of planning a child:
- talk to your doctor before you stop taking contraceptive agents;
- valproate treatment should never be discontinued without the recommendation of the attending physician, as the patient's condition may worsen.

If the patient taking valproate becomes pregnant:
- she should not stop taking valproate as this may exacerbate symptoms of epilepsy or bipolar affective disorder;
- she should immediately discuss the available options with her doctor and obtain the necessary information. The doctor will explain whether a change in treatment is necessary and how it should be carried out.

Treatment should be regularly consulted with a specialist – at least once a year.

[logo]

At the start of treatment and at the annual visit, both the patient and the specialist read and sign an annual risk acknowledgement form. This is to ensure that the patient knows and understands the risks associated with the use of valproate during pregnancy and also understands the need to prevent pregnancy while taking valproate.

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MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

2 What are the risks to the child of taking valproate during pregnancy?

[Picture]

The higher the dose, the higher the risk, however, all doses are dangerous.

Taking valproate during pregnancy may cause serious birth defects.

In women taking valproate during pregnancy, a birth defect occurs in about 11 children per 100, while in the general population, the rate is approximately 2-3 children per 100.

What types of birth defects may occur?

Reported birth defects related to the use of valproate include, but are not limited to:

- malformations of bone tissue of the spine (spina bifida);
- malformations of the face and skull – including cleft lip and palate;
- malformations of the limbs, heart, kidneys, urinary tract, genitals and eyes that may affect the ability to see;
- hearing problems or deafness.

Taking valproate during pregnancy may affect the development of the child's nervous system during adolescence.

30 to 40 out of 100 pre-school children may develop neurodevelopmental problems such as:

- delayed learning of walking and speech;
- lower level of intelligence compared to other children of the same age;
- speech and language skills disorders;
- memory problems.

Children are at increased risk of developing autism or autism spectrum disorders, as well as of developing attention deficit disorder and/or attention deficit hyperactivity disorder.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

3 Contraception (birth control)

[logo]

Throughout the entire period of valproate treatment an effective method of contraception (birth control) prescribed by a doctor must be used

This is to prevent pregnancy during the treatment with valproate, as it can have harmful effects on the child.

[logo]

Consult your attending physician, gynaecologist/obstetrician or midwife for advice on the optimal method of contraception.

Contraception must also be used by patients who are not currently sexually active, unless there are justified reasons to assume that there is no risk of getting pregnant. The specialist should discuss this issue with the patient.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

4 I am an adult person, what does this mean for me?

"I AM STARTING TREATMENT WITH VALPROATE"

[logo]

The specialist will explain why valproate is an appropriate medication for the patient and will also discuss with her all the known risks. A specialist should only start treatment with valproate if no other drugs are effective .

- The patient should only be treated with valproate if she is not pregnant and is using an effective method of contraception (birth control).
- The doctor will ask the patient to take a pregnancy test and advise on the choice of an appropriate method of contraception.
- Treatment should be regularly consulted with a specialist – at least once a year.

[logo]

At the start of treatment and at the annual visit, both the patient and the specialist read and sign an annual risk acknowledgement form. This is to ensure that the patient knows and understands the risks associated with the use of valproate during pregnancy and also understands the need to prevent pregnancy while taking valproate.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

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"I TAKE VALPROATE

AND I DON'T PLAN ON GETTING PREGNANT"

[logo]

The patient should always use effective contraception (birth control), even if she is not currently sexually active:

- **contraception should be used throughout the entire time valproate is taken;**
- **contraceptive agents should not be discontinued at any time.**

[logo]

If the patient needs advice on contraception, she should consult her attending physician, gynaecologist/obstetrician or midwife/family planning clinic staff.

Inform your doctor immediately if you are pregnant or suspect that you may be pregnant.
Do not discontinue valproate or contraception without consulting your doctor.

Regularly consult the treatment with a specialist – at least once a year. At the annual visit, both the patient and the specialist read and sign an annual risk acknowledgement form. This is to ensure that the patient knows and understands the risks associated with the use of valproate during pregnancy, and understands the need to prevent pregnancy while taking valproate.

[logo]

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

[logo]

"I TAKE VALPROATE

AND I AM PLANNING TO GET PREGNANT"

Do not discontinue contraception (birth control) or valproate without consulting your doctor.

- A specialist may find it necessary to replace valproate with another drug well before getting pregnant to ensure that the disease is stable.
- It is very important not to get pregnant before discussing this issue with a specialist.
- Treatment should be regularly consulted with a specialist – at least once a year.

[logo]

At this visit, both the patient and the specialist read and sign an annual risk acknowledgement form. This is to ensure that the patient knows and understands the risks associated with the use of valproate during pregnancy and also understands the need to prevent pregnancy while taking valproate.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

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[logo]

“I TAKE VALPROATE AND I AM PREGNANT OR SUSPECT, THAT I MAY BE PREGNANT"

Valproate should not be discontinued as this may exacerbate symptoms of epilepsy or bipolar affective disorder.

[logo]

The patient should discuss the available options **with the specialist immediately** and obtain the necessary information. The specialist will explain whether a change in treatment is necessary and how it should be carried out.

Infants of mothers who were taking valproate during pregnancy are at increased risk:

- birth defects and
- problems related to nervous system development and learning.

Both of these factors can seriously affect a child's life.

[Picture]
[logo]

The patient will be monitored very closely.

- This is to ensure that the disease remains under control.
- This will also enable the assessment of the child's

At this visit, both the patient and the specialist read and sign an annual risk acknowledgement form. This is to ensure that the patient knows and understands the risks associated with the use of valproate during pregnancy.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

5 I am a girl (any age)

[logo] For your epilepsy your doctor has prescribed valproate, which is an important medication that ensures your well-being.

[logo] Children of mothers treated with valproate may have very serious health problems.

You may want to have a child one day.
Therefore, you must carefully follow the recommendations below.

I am not menstruating yet

As soon as you start menstruating, inform your parents/legal guardians about it.
You will need to talk to your doctor about the applied treatment.

I am already menstruating

The doctor will make sure that you are not pregnant.

Your doctor will prescribe a medication to prevent you from getting pregnant, known as a contraceptive, even if you are not sexually active.
You should use contraception throughout the entire period of taking valproate.

I am pregnant or suspect that I may be pregnant

Contact your doctor immediately.
The doctor will determine the appropriate management.
Do not stop taking valproate without consulting your doctor.

[logo] In any case, you must see your doctor at least once a year. During the visit, the doctor:

- will check whether valproate is still the right medication for you,
- will discuss valproate treatment with you and
- will ask you (or your parents/legal guardians) to sign a document confirming that you understand all the recommendations you have received.

[logo] If you have any questions, ask your attending physician or your parents/legal guardians.

Do not stop taking valproate without talking to your doctor.

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A GUIDE FOR MALE PATIENTS ON VALPROATE

For full product information, read this guide together with the leaflet for the patient

VALPROATE, WHAT YOU NEED TO KNOW

This guide provides key information on the potential risks of using valproate in male patients during the 3 months before conception. Consult with your doctor or pharmacist if you have any questions.

KEEP THIS GUIDE, SO THAT IT CAN BE REREAD IF NECESSARY.

Information on the use of valproate in male patients can also be found online at www.walproiniany.pl

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What risks are associated with taking valproate in the period of conception of a child

A study has been conducted that suggests a possible risk of motor disorders and disorders of mental development (developmental problems in early childhood) in children of fathers treated with valproate within the 3 months before conception.

In this study, about 5 out of 100 children whose fathers were treated with valproate had such disorders, compared with about 3 out of 100 children of fathers treated with lamotrigine or levetiracetam (other drugs that may be used to treat the patient's disease).

However, the study has limitations and therefore it is not entirely clear whether the increased risk of impaired motor and mental development suggested by this study is caused by valproate. The study assessed a wide range of motor development and mental health disorders. However, the study was not large enough to demonstrate which specific type of disorder in children is associated with the existing risk.

For example, disorders of motor and mental development when growing up can include:

- mobility problems
- lower intelligence than in other children of the same age
- speech and language skills disorders
- autism or autism spectrum disorders
- attention deficit hyperactivity disorder

In children of fathers who discontinued valproate treatment at least 3 months (the time required to produce new sperm) before the conception, the risk is unknown.

What does this mean for me?

As a precaution, the doctor will discuss with the patient the potential risks to the children of fathers treated with valproate within 3 months before the conception.

The doctor will also discuss the following issues with the patient:

- the need for the patient and his female partner to consider the use of effective contraception (birth control) during valproate treatment and for 3 months afterwards (the time needed to produce new sperm);
- the need to consult a doctor when planning to conceive a child and before discontinuing contraception (birth control);
- the possibility of using other methods to treat the disease, depending on the individual situation.

Do not donate semen while taking valproate and for 3 months after it has been discontinued. If you are planning to have a child, talk to your doctor.

If the patient's female partner becomes pregnant and the patient has used valproate within 3 months prior to conception and has questions related to it, he should contact a doctor.

Do not discontinue treatment without consulting your doctor. If the patient discontinues treatment, symptoms may worsen.

MORE DETAILED INFORMATION IS PROVIDED IN THE PATIENT INFORMATION LEAFLET

Patient chart on valproate

▼ Valproate – this medicinal product will be additionally monitored. This will enable new information on the safety of the drug to be identified quickly. The user of the medicine can also help by reporting any adverse reactions that occurred after using the medicine (see section 4 of the package leaflet).

What you need to know and do

All girls and women who use valproate and are capable of becoming pregnant:

- valproate can seriously harm the unborn child if taken by the mother during pregnancy;
- an effective method of contraception should be used continuously throughout the entire period of treatment with valproate;
- if you suspect that you may be pregnant, make an appointment with your doctor immediately;
- you should visit a specialist at least once a year.

Male patients using valproate:

- risk of motor and mental development disorders is possible in children of men treated with valproate within 3 months before conception;
- discuss these possible risks and the need for effective contraception with your doctor.

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Patient chart on valproate

What you need to know and do

- Valproate is an effective substance in the treatment of epilepsy and bipolar affective disorder.

This applies to all girls and women who use valproate and are capable of becoming pregnant and to male patients using valproate:

- read the leaflet carefully before use;
- never discontinue valproate unless advised by your doctor, as your condition may worsen;
- talk to your doctor if you are considering becoming pregnant; do not stop taking valproate and do not stop using an effective method of contraception until this conversation has taken place;
- ask your doctor to make the Patient Guide available to you. More information on the use of valproate can be found at www.walproiniany.pl.

Keep this card safe so that you always know how to proceed.

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Annual risk acknowledgement form

▼This medicinal product will be additionally monitored. This will enable new safety information to be identified quickly. Healthcare professionals are asked to report any suspected adverse reactions (see section 4.8 of the Summary of Product Characteristics).

Annual risk acknowledgement form for girls and women of childbearing age treated with valproate

Please read, complete and sign this form when you visit your specialist: at the start of your treatment, at your annual visits, and if you are planning pregnancy or becoming pregnant. This is to ensure that the patient or her legal guardian/representative have discussed with the specialist and understood the risks associated with the use of valproate during pregnancy.

Part A — To be completed and signed by

Name of the patient or her legal guardian/representative:

I confirm that the patient named above requires treatment with valproate because:

- this patient does not respond sufficiently to other drugs or ..... ☐
- this patient is intolerant to other medicines. ..... ☐

I have discussed the following information with the patient named above or her legal guardian/representative:

- The general risks for children exposed to valproate during pregnancy are: ..... ☐
  - approximately 11% risk of major birth defects and
  - 30-40% risk of developing a range of early developmental disorders that may lead to delayed psychomotor development.
- Valproate should not be used during pregnancy (except in rare cases of epileptic patients who are found to be resistant or intolerant to other drugs) and the terms of the pregnancy prevention programme should be followed. ..... ☐
- The need to have regular (at least once a year) follow-up examinations and to assess the need for continuation of valproate treatment with a specialist. ..... ☐
- The need for a negative pregnancy test result prior to the start of treatment and thereafter, according to the requirements (in patients of childbearing age) ..... ☐
- The need for continuous use of an effective method of contraception throughout the entire period of valproate treatment (in patients of childbearing age) ..... ☐
- The need to make an appointment with a doctor as soon as a pregnancy has been planned, to allow the early discussion of available treatment options and changes to other possible methods of treatments prior to getting pregnant and before discontinuation of contraception ..... ☐
- The need to contact a doctor immediately for an urgent treatment assessment in the case of suspected pregnancy or confirmation of unplanned pregnancy. ..... ☐
- I have given the patient or the legal guardian//representative a copy of the Patient Guide. More information on the use of valproate can be found at www.walproiniany.pl
- In the case of pregnancy, I confirm that this pregnant patient:
  - has received the lowest possible effective dose of valproate to minimise the possible harmful effects on the foetus ..... ☐
  - has been informed of the possibility of receiving support or counselling on pregnancy and appropriate monitoring of her child's health in the event of pregnancy ..... ☐

Name and surname of the specialist	Signature	Date

This form will be given by the specialist to girls and women of childbearing age who are being treated with valproate for epilepsy or bipolar affective disorder (or their legal guardians/ representatives).

Parts A and B of the form should be completed: all relevant boxes should be ticked and the form should be signed; this is to confirm that all risks and information associated with the use of valproate during pregnancy have been understood.

A completed and signed copy of this form will be kept/recorded by the specialist.

It is recommended that the prescribing physician saves an electronic version of the form in the patient's medical records. A completed and signed copy of this form will be given to the patient to keep.

▼ Valproate - this medicinal product will be additionally monitored. This will enable new information on the safety of the drug to be identified quickly. The user of the medicine can also help by reporting any adverse reactions that occurred after using the medicine (see section 4 of the Package Leaflet).

Annual risk acknowledgement form for girls and women of childbearing age treated with valproate

Please read, complete and sign this form when you visit your specialist: at the start of your treatment, at your annual visits, and if you are planning pregnancy or becoming pregnant. This is to ensure that the patient or her legal guardian/representative have discussed with the specialist and understood the risks associated with the use of valproate during pregnancy.

Part B To be completed and signed by the patient or legal

I have discussed with the attending specialist and understood the following information:

.....

.....

- Reasons why I require treatment with valproate instead of another drug ..... ☐
- The need to make regular (at least once a year) visits to a specialist in order to check whether valproate treatment is still the best therapeutic option in my case ..... ☐
  - Risks to children whose mothers were taking valproate during pregnancy are: ..... ☐
  - approximately 11% risk of major birth defects and
  - 30-40% risk of developing a range of early developmental disorders that may lead to delayed psychomotor development.
- The need for a negative pregnancy test result prior to the start of treatment and thereafter, according to the requirements (if I am of childbearing age) ..... ☐
- The need for continuous use of an effective method of contraception throughout the entire period of valproate treatment (if I am of childbearing age) ..... ☐

- We have discussed the possible methods of effective contraception or have scheduled a consultation with a specialist experienced in counselling on effective contraception ..... ☐
- The need to have regular (at least once a year) follow-up examinations and to assess the need for continuation of valproate treatment with a specialist ..... ☐
- The need to have a consultation with my doctor as soon as I plan to become pregnant, so that the treatment options available to me can be discussed early enough and can be changed to other possible methods of treatment before I become pregnant and before I stop using contraception ..... ☐
- The need to consult a doctor urgently if I suspect I may be pregnant. ..... ☐
- I have received a copy of the Patient Guide. More information on the use of valproate can be found at www.walproiniany.pl

In the case of pregnancy, I have discussed the following information with the attending specialist and I understand:

- the possibility to receive support or counselling on pregnancy, ... ☐
- the need for appropriate monitoring of my child's health if I become pregnant ..... ☐

Name and surname of the patient or legal guardian/ representative	Signature	Date

This form will be given by the specialist to girls and women of childbearing age who are being treated with valproate for epilepsy or bipolar affective disorder (or their legal guardians/ representatives).

Parts A and B of the form should be completed: all relevant boxes should be ticked and the form should be signed; this is to confirm that all risks and information associated with the use of valproate during pregnancy have been understood.

A completed and signed copy of this form will be kept/recorded by the specialist.

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ADR Reporting

Suspected Adverse Drug Reactions or medication errors should be reported to the Malta Medicines Authority via the ADR reporting form, available online at http://www.medicinesauthority.gov.mt/adrportal.

The ADR reporting form can be sent by post to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or via email to postlicensing.medicinesauthority@gov.mt.

Alternatively, adverse drug reactions can also be reported to Central Procurement & Supplies Unit, (Head Office),UB002, Industrial Estate, San Gwann - SGN3000 or via email: info.cpsu@gov.mt.