

Benefits and risks of taking antiepileptic medicine for females

Information for healthcare professionals



This booklet provides information for you, as a healthcare professional, to:

- Understand the risk of harm to an unborn child when a female is taking antiepileptic medicines for any indication.
- Support your responsibilities to educate female patients considering or taking antiepileptic medicines.

It is clearly established that antiepileptic medicines are associated with congenital malformations (such as spina bifida, cleft palate and heart defects), cognitive impairment and behavioural difficulties (such as Autistic Spectrum Disorder).

When dysmorphic features are combined with other malformations some people use the term ‘Foetal Anticonvulsant Syndrome’.



Contents

| | | | |
|--|----|--|----|
| Key messages | 3 | More information | 12 |
| The risks of taking antiepileptic medicines during pregnancy | 4 | Order this booklet | 12 |
| How can the risk be minimised? | 5 | National support services in New Zealand | 12 |
| Advice to patients | 10 | Reporting an adverse drug reaction | 13 |
| Checking you have been clear | 11 | Reference list | 13 |
| Parents concerned about whether a child has been affected | 11 | Appendix 1: Contraceptives in Epilepsy | 14 |

Key messages

- All antiepileptic medicines taken in pregnancy have the potential to harm an unborn child.
- Advise your female patient on the importance of two effective forms of contraception, if they are of childbearing age and potentially sexually active.
- Identify and annually review your female patients taking antiepileptic medicines. Check the appropriateness of antiepileptic medicines, and reinforce relevant messaging. Clearly document your review and the discussion.
- Advise female patients of the importance of planning a pregnancy in consultation with a doctor or specialist.
- It is the prescriber’s responsibility to ensure that all their female patients are aware of the risks associated with taking antiepileptic medicines while pregnant.
- Do not prescribe sodium valproate to sexually active females of child bearing age unless there is no reasonable alternative as sodium valproate has the highest risk of harm.
- In the event of an unplanned pregnancy while taking antiepileptic medicines, advise your patient to continue their medicines, and that you will seek urgent specialist advice.
- We have produced the booklet “Are you taking medicines for epilepsy, mood or pain? Information for females, their family and whānau” to help you go through these risks with your patient.

The risks of taking antiepileptic medicines during pregnancy

Antiepileptic medicines are used to manage epilepsy, mental illness and pain. All antiepileptic medicines have the potential to harm an unborn child. The risks vary depending on the antiepileptic medicine but fall into two main categories: congenital malformations and neurodevelopmental effects.

Increased rates of congenital malformations are reported from Epilepsy Pregnancy Registries (4-7% compared to 2-3% in the general population). Risks are greatest with sodium valproate (10%; 24% with high doses >1500mg/day respectively), topiramate and phenobarbital, and lower with carbamazepine, lamotrigine and levetiracetam. Polytherapy that includes sodium valproate carries the highest overall risk.

The Epilepsy Pregnancy Registry sample sizes are generally too small to determine if specific types of malformations can be attributed to specific antiepileptic medicine exposure but there are case reports of malformations of most body systems.

Neurodevelopmental effects of antiepileptic medicines are established for sodium valproate. Children born to mothers taking sodium valproate (>800mg/day) in pregnancy have an average decrease in IQ of 7-10 points. They are 8 times more likely to require educational intervention at 6 years of age. Four percent of children exposed to sodium valproate in utero have Autistic Spectrum Disorder compared to 2% in children that are not exposed.

How can the risk be minimised?

The specific risk from antiepileptic medicines can only be reduced by decreasing the dose or changing the medicine.

However, any reduction in risk to the unborn child must be balanced against the risk for the mother of changing dose or medicine.

This is particularly important in **epilepsy**, where the risks of change may be significant. Decreasing or changing the antiepileptic medicine may cause loss of seizure control. There is a risk of status epilepticus if the antiepileptic medicine is weaned quickly. Seizures themselves can have a negative effect on an unborn child, including hypoxia or miscarriage. Loss of seizure control for your female patient may result not only in significant deterioration in quality of life but also substantially increases risk of death. Women with epilepsy die of Sudden Unexplained Death in 1 in a 1000 pregnancies. The only way to decrease this risk is to control seizures. There is also a 10-fold increased risk in maternal death due to status epilepticus. For these reasons any changes to the antiepileptic medicine in a patient with epilepsy should be made in consultation with a neurologist or paediatrician.

Because of the increased risk of major congenital malformations and adverse neurodevelopmental outcomes, sodium valproate should not be prescribed for the long-term treatment of mental health disorders in females of childbearing potential.



Including your patient in this decision making is important.

Non-pregnant females on antiepileptic medicines

If a non-pregnant female patient is taking an antiepileptic medicine, consider a reduction in dose or a change to a medicine with lesser risk. Including your patient in this decision making is important.

The risk of change is relatively low in patients with mood disorder, pain and headache, but relatively high in patients with epilepsy (page five). Therefore, any change should be discussed with a relevant specialist (usually a neurologist, psychiatrist or paediatrician). If the patient is actively considering pregnancy or is at high risk of accidental pregnancy, then this needs to be done **urgently**.

Any female who could be sexually active should be advised and encouraged to use effective contraception. Antiepileptic medicines can interact with hormonal contraception so prescribe a double method of effective contraception. Consider referral for expert contraceptive advice [See Appendix 1].

Females of childbearing potential must have yearly reviews of their medicines so that the patient receives a regular review of what they already know about the importance of effective contraception and planning a pregnancy. It is also important for you to review the appropriateness of the medicines for the patient's condition.

Non-pregnant females on antiepileptic medicines planning a pregnancy

As soon as a female patient starts planning a pregnancy advise them to take folic acid 5mg daily to reduce the background risk of neural tube defects.

Pregnant females on antiepileptic medicines

If a patient becomes pregnant while already taking an antiepileptic medicine, the potential to reduce risk is limited, as the major effects occur early in the first trimester. However the effects of sodium valproate on the child's cognition may occur at any time in the pregnancy.

In patients with epilepsy, do not make a change to their antiepileptic medicine or withdraw it without discussion with a neurologist or paediatrician, as this carries substantial risk for mother and baby.

In patients using the medicine for mood stabilisation or pain, seek advice on an alternative medicine.

Consult with the appropriate specialist within 48 hours. This will usually be a neurologist, psychiatrist or possibly paediatrician. Refer for a consultation with an obstetrician as well.

All members of your patient's healthcare maternity team need to communicate clearly with each other and the patient because of the nature of the risks involved. All information needs to be shared between primary care and your patient's Lead Maternity Carer.

Considerations required for starting antiepileptic medicines

Epilepsy: Do **not initiate** a new prescription for **sodium valproate** in a sexually active female of childbearing age for focal epilepsy unless all reasonable alternative treatments have been tried and have failed, or have not been tolerated.

For the generalised epilepsies, such as Juvenile Myoclonic Epilepsy, sodium valproate is known to be the most effective antiepileptic medicine. Lamotrigine and levetiracetam are less effective, but can provide good control in some patients and can be tried at reasonable dose first. However, if control is not promptly achieved, then sodium valproate may be necessary. Females with generalised epilepsies should be given information on the possible antiepileptic medicine options including their likely effect on seizures as well as their likely impact on any future pregnancies so that they are well informed when choosing an antiepileptic medicine. Remember to always check you have been clear at the end of any discussion with the patient.

Headache, pain or mood disorder: Do **not initiate** a new prescription for an antiepileptic medicine in any sexually active female of childbearing age without considering the risks and benefits of the medicine to the female patient and discussing this with them.

Advice to patients

All female patients initiating or already taking antiepileptic medicine (and their parents or guardians if minors) should be given information about the:

- risks of antiepileptic medicine in pregnancy and the fact the impact is highest early in the first trimester often before they know they are pregnant.
- importance of two forms of effective contraception if sexually active (remember that the efficacy of hormonal contraceptives can be reduced by the concurrent use of antiepileptic medicines). Discuss a double form of contraception and referral for expert contraceptive advice with the patient [See Appendix 1].
- importance of a planned pregnancy with medical input 6-12 months in advance of getting pregnant.
- need to take folic acid 5 mg daily when trying to conceive and through the first trimester.
- risks of not treating or of changing treatment to both themselves and their unborn child.

Use the “Are you taking medicines for epilepsy, mood or pain? Information for females, their family and whānau” booklet in your discussion with your patient and their family and whānau.

Information regarding the risks of antiepileptic medicine on an unborn child **must be** given to all females (and the parents or guardians of younger females) regardless of their age, until your patients are beyond child bearing age. This way when younger patients become sexually active they are already aware of the risks and the need for effective contraception. Annually review and discuss the risks with your female patients.


Checking you have been clear

Evidence suggests that some healthcare professionals think they have been clear with patients but patients do not always understand what they have been told.


Checking you have been clear is the third step in the Three Step Model to better health literacy published by the Health Quality & Safety Commission.

For more information refer to:

The Health Quality & Safety Commission's three steps to better health literacy

 <http://safer.nz/STBHL>

U.S. evidence

 <http://safer.nz/PMC3037129>

Parents concerned about whether a child has been affected

If you have a patient who is concerned that an existing child may have been affected by antiepileptic medicines during a previous pregnancy, consider a referral to a paediatrician.

More information

Remember to use local support networks in your region.

More information on medicines is available from

www.Medsafe.govt.nz or www.nzformulary.org

Different risks of harm

<http://safer.nz/Dec14SodVal>

Sodium valproate in pregnancy

<http://safer.nz/Sep15SodVal>

Epilepsy in pregnancy

<http://safer.nz/EpiPreg>

Health Navigator

www.healthnavigator.org.nz/

Order this booklet

To order printed copies of this booklet please email treatmentinjury@acc.co.nz

National support services in New Zealand

Epilepsy Association of New Zealand

www.epilepsy.org.nz

Ph: 0800 374 537

Email: national@epilepsy.org.nz

Mental Health Foundation

www.mentalhealth.org.nz

Ph: (09) 623 4810

Email: info@mentalhealth.org.nz

Family Planning

www.familyplanning.org.nz

Email: national@familyplanning.org.nz

Foetal Anti-Convulsant Syndrome NZ

www.facsnz.com

Ph: 021 189 4483

Email: denise@facsnz.com

Reporting an adverse drug reaction

| | |
|-------------|---|
| Phone | + 64 3 479 7247 to speak to a Medical Assessor at the Centre for Adverse Reactions Monitoring (CARM) |
| Online | Submit a report to CARM https://nzphvc.otago.ac.nz/report/ |
| Yellow Card | A completed Yellow Card can be submitted to CARM via email, fax or mail which can be obtained from contacting CARM. |
| Email | carmnz@otago.ac.nz |
| Fax | +64 3 479 7150 |

Reference list

Epstein, R. A., et al (2015). Treatment of bipolar disorders during pregnancy: Maternal and fetal safety and challenges. *Drug, Healthcare and Patient Safety*, 7, 7–29.

Meador, K. J., & Loring, D. W. (2016). Developmental effects of antiepileptic drugs and the need for improved regulations. *Neurology*, 86, 1–10.

Tomson, T., et al. (2015). Valproate in the treatment of epilepsy in girls and women of childbearing potential. *Epilepsia*, 56(7), 1006–1019.

Appendix 1: Contraceptives in Epilepsy

This guide relates specifically to contraceptive/antiepileptic medicine interactions. It does not take into consideration other factors that may influence contraceptive eligibility.

Enzyme Inducers

Preferred options = no interaction :-

- Copper IUD
- Mirena/Jaydess
- Depo Provera

Contraceptive efficacy reduced :- classed as MEC3 (risk probably outweighs benefits)

- Combined Hormonal Contraception
- Progestogen Only Pill
- Implant

NB

For emergency contraception postcoital IUD is the most effective method.

Efficacy of the emergency contraceptive pill is reduced and requires doubling the dose of levonorgestrel – ie postinor-1 (1.5 mg tablet) x 2 tablets stat.

Lamotrigine

Preferred options = no interaction :-

- Copper IUD
- Mirena/Jaydess
- Depo Provera
- Implant

Level of lamotrigine possibly reduced – increased seizure risk :-

Combined Hormonal Contraception

Level of lamotrigine possibly increased – increased risk of adverse effects :-

- Progestogen Only Pill – Desogestrel

All other antiepileptic drugs

All contraceptive options can be considered, check with New Zealand Formulary Interaction Checker – www.nzf.org.nz

Benefits and risks of taking antiepileptic medicine for females

Published: September 2017

Review date: September 2019

Review managed by: Treatment Safety, ACC
ACC7809

This information is intended to provide guidelines and general advice to healthcare professionals, but should not be used as a substitute for assessment with the circumstances that are relevant to the individual patient.



Helping females and their families
understand the risks and benefits of taking
antiepileptic medicines.

