Participant Information Sheet

Study title:	**The EpiNet-*First* trials of new onset epilepsy**		
Locality:	**Auckland District Health Board**	Ethics committee ref.:	**14/NTB/56**
Lead investigator:	**Dr Peter Bergin**	Contact phone number:	**09 379 7440 ext 25663**

You are invited to take part in a research study to find out which of several anti-epileptic drugs is best for people who are starting treatment for epilepsy. It is up to you to decide whether to take part. If you do not want to take part, you do not have to, and you do not have to give a reason. You will still receive normal care for your epilepsy. If you want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It explains why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what will happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this. You are able to take as much time as you like deciding whether to participate in the study (though there may be a risk of further seizures while you are not taking any treatment.)

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep. We will want to follow you for at least 2 years.

This document is 8 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

Epilepsy is a common neurological (brain) disorder. Approximately 2-3% of the population will be given a diagnosis of epilepsy by the time they reach 60.

There are many drugs (i.e. medications) which are available to treat patients with epilepsy. All of these drugs have been shown to be helpful in reducing the likelihood of seizures, though they do not necessarily prevent all seizures in all patients. Unfortunately, doctors cannot always predict which medication will work best for a particular person. In fact, some of them seem to have no effect at all in some patients.

In this research study - called The EpiNet-*First* series of trials - we want to find out which of the various anti-epileptic drugs work best in people with new-onset epilepsy.

We will not be able to obtain enough patients in New Zealand alone to answer this question fully. This is therefore an international study.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

You have been invited because your doctor thinks you have developed epilepsy. Your doctor thinks you should start treatment with an anti-epileptic drug.

If you agree to take part, then we will need to collect information about your epilepsy. Your doctor will fill in a form via the Internet to tell us what sort of seizures you have had, and whether you have other health problems. Information will be transmitted via the Internet using a secure website, similar to those that are used by banks. We will not be collecting any personal information about you, apart from your name, date of birth, sex and hospital number. No material which could personally identify you will be used in any reports on this study.

You will not need extra blood tests or any other samples taken for the study. Your doctor will decide what tests or investigations (e.g. EEG or brain scan), if any, you should have.

If you agree to take part, neither you nor your doctor will choose which anti-epileptic drug you receive. Instead, the treatment you will be offered will be chosen at random (by a computer, in a way that is similar to tossing a coin or rolling a dice). Once you have been allocated an anti-epileptic drug both you and your doctor will know what it is.

If drugs are randomly chosen, then we can be confident that the groups of patients who receive the different drugs will be very similar. We can then follow the groups of patients to see if one group has a better outcome than the other groups.

All of the drugs we are studying have been used in New Zealand for many years, and are approved for the treatment of epilepsy. We know that they work well for most people. We are now trying to find out if one is better than the others.

If your doctor has diagnosed you as having focal seizures (seizures that begin in one part of the brain), you will be enrolled into the **EpiNet-*First* Trial 1**. You will receive treatment with either carbamazepine, lamotrigine or levetiracetam.

If your doctor has diagnosed you as only having generalized seizures, you will be enrolled into the **EpiNet-*First* Trial 2.** You will receive treatment with either levetiracetam or valproate.

If you have only generalized seizures, but valproate is not considered appropriate, you will be enrolled into the **EpiNet-*First* Trial 3.** You will receive treatment with either levetiracetam or lamotrigine.

If your doctor has diagnosed you as having epilepsy, but it is unclear what type of seizures you have, you will be enrolled into the **EpiNet-*First* Trial 4.** You will receive treatment with either levetiracetam or lamotrigine or valproate.

The **EpiNet-*First*-Trial 5** is for patients with seizures of uncertain nature for whom valproate is not appropriate. You will receive treatment with either levetiracetam or lamotrigine.

After treatment has been started you will be followed up at 3, 6 and 12 months, and at 6 month intervals thereafter, depending on how well you are responding to treatment. For some of these follow-ups, we will see you in a clinic, but for other reviews we may contact you by phone or e-mail.

You will also be asked to complete a brief questionnaire at the start of your treatment and again after 3 months, and then at 6 month intervals for at least the next 2 years.

You will be asked to keep a diary of any seizures that may occur. In particular, we will want to know whether you have further seizures, and if so, how often they occur. **It is important that you record all the seizures you have as accurately as you can.** We will also want to know whether you experience side effects from the treatment, and if so, how severe they are. If it turns out that the treatment does not control your seizures, or causes major side effects, the treatment can be stopped and another treatment started. If this happens we would still like to collect information about your progress.

To ensure that the information we collect is meaningful, **it is very important that you do actually take the medication you are prescribed as reliably as possible**. You can stop the medication if you have troublesome side effects, or if you change your mind, but **we need to know if you stop taking it**. We could be misled if patients do not take the medication prescribed, and we do not know this, because we could draw the wrong conclusion about the effectiveness of the different medications. If you experience troublesome side effects, tell your doctor, and discuss with him or her whether you should continue it.

The study will start in 2014 and we plan to recruit over 3,600 patients with epilepsy (internationally and over the five EpiNet-*First* trials); we wish to follow up everyone who has taken part in the study for at least 2 years.

Your usual treatment will not be affected by taking part in this study and you will receive routine clinical care.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

What are the side effects of the antiepileptic drugs being tested?

We will not be giving you any experimental drugs. All the drugs that we are using are standard medications that are known to be safe and effective in people with epilepsy; they are registered in New Zealand for the treatment of epilepsy, and are approved by New Zealand's drug supervising agency, Medsafe, for this purpose.

However, there are side effects to all types of medicines and there is still a small risk that you could have some sort of adverse reaction to a medication, though this risk will not be increased by taking part in the research study. In other words, you are likely to have the same risk, even if you do not take part in this trial. Similarly, there is a very small chance that a person with epilepsy can die during a seizure; however, once again, this risk will not be increased by taking part in the research study.

Side effects

Some anti-epileptic drugs may cause dizziness, sedation (sleepiness), nausea or diarrhoea, clumsiness, or double or blurred vision in some patients, particularly if the dose is too high. However, many people do not get any side effects from their anti-epileptic medicine, particularly if the medicine is introduced slowly. If side effects do occur, they often settle over the first few days or weeks after a patient starts the drug. Occasionally, anti-epileptic drugs can cause mood changes; sometimes people feel less motivated or less enthusiastic about their activities. Some people put on weight or get thinning of the hair with anti-epileptic drugs. Some drugs can cause a reversible tremor.

If you develop any of the side effects mentioned here, or any other possible side effects, and you are concerned, you should contact your hospital doctor or nurse (contact details can be found on your seizure diary).

Allergies and hypersensitivity reactions
Some people turn out to be allergic to one or more anti-epileptic drugs. Allergic reactions most commonly happen in the first few weeks after the treatment is started. The most common sign of an allergy is a skin rash. This is most likely with carbamazepine and lamotrigine; approximately one in twenty people will develop a skin rash with each of these drugs. Patients typically develop a rash that looks like a measles rash. The rash is usually a minor nuisance, but it can develop into a more severe allergic reaction. If you develop a rash you should contact your hospital doctor or nurse (contact details can be found on your seizure diary). If you cannot get hold of anyone, and you have a rash that is getting worse, you should stop the drug immediately. Some genetic factors seem to increase the risk of a serious allergic reaction to carbamazepine, particularly in Asian patients.

Sexuality and reproductive issues for women
There is an interaction between some anti-epileptic drugs and the combined oral contraceptive pill. Carbamazepine reduces the effectiveness of oral contraceptives, and lamotrigine may also do so. Women who are sexually active and taking carbamazepine or lamotrigine should therefore consult their doctor or family-planning services before stopping or starting an oral contraceptive medication. Levetiracetam and valproate do not interact with the oral contraceptive pill.

Women may develop irregular periods with valproate.

Most anti-epileptic drugs increase the risk to an unborn baby.These risks must be balanced against the risks of uncontrolled seizures. If you have any questions or concerns, your hospital doctor will discuss this further with you.

Anti-epileptic drugs may cause abnormalities in the baby called congenital malformations. These might include a cleft lip, cleft palate, heart defects, or spina-bifida. For lamotrigine, carbamazepine and levetiracetam the risk is about 3% (3 in 100). For valproate the risk may be as high as 10% (1 in 10). There is also evidence that valproate may result in the baby having learning difficulties. For these reasons, we do not recommend that women of childbearing age take valproate, if they are in a sexual relationship.
When the drug allocated to you is dispensed there will be a full information sheet in the packaging which is supplied by the manufacturer. This sheet will add to the information given about your drug in this Participant Information Document.

What are the possible disadvantages and risks of taking part?
There are risks associated with epilepsy, and risks associated with the medicines that are prescribed to control epilepsy, but there are no risks that are directly associated with the research itself. You may end up taking a medication that is different from the one your doctor would have prescribed if you were not taking part in this research. It is possible that you may have a worse outcome - either because of side-effects, or because the medication prescribed is less effective than the one you would otherwise have received. On the other hand, you may have a better outcome. The reason we are doing the study is to find out which of the medications is best. If you have been invited to take part in this study, then your doctor thinks that any of the medications you might receive would be appropriate for you.

What are the benefits of taking part?
By taking part you will help doctors learn whether one of the drugs we use to treat epilepsy is better than the other drugs. We hope that the results of this study will help us to improve the treatment of epilepsy in the future.
We cannot say if you will benefit directly from this research study yourself; you may end up taking a drug that is less effective or has a higher risk than another drug, or you may end up taking a drug that is shown to be the best one. You will be monitored more closely than would be the case if you did not take part in this research study.
If you wish, you may ask a friend, family or whanau member to help you understand the risks and / or benefits of this study and any other explanation you may require. If you need an interpreter, one can be provided, though this may require that you come back to another appointment.

WHO PAYS FOR THE STUDY?

The study is funded by the Neurological Foundation of New Zealand and the New Zealand Health Research Council. It is being run in your hospital, and is being organised by The EpiNet steering group and the Auckland District Health Board.

You can find out more about the EpiNet Research Project at this website: www.epinet.co.nz

There will not be any costs to you for participating, nor any payments made to you.

WHAT IF SOMETHING GOES WRONG?

If you have any concerns about any aspect of this study, you should speak with your hospital doctor (consultant).

If you were injured as a result of treatment given as part of this study, which is unlikely, you would be eligible for compensation from ACC just as you would be if you were injured in an accident at work or at home. You will have to lodge a claim with ACC. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

If harm occurs to you and is due to someone's negligence, you may have grounds for legal action for compensation against the treating District Health Board or Hospital. In the event of a defective product you may have grounds for legal action for compensation against the manufacturer. However, in both cases you may have to pay your legal costs.

If you have any queries or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate, telephone

- Northland to Franklin 0800 555 050
- Mid and lower North Island 0800 42 36 38 (4 ADNET)
- South Island except Christchurch 0800 377 766
- Christchurch 03 377 7501

WHAT ARE MY RIGHTS?

Will my taking part in this study be kept confidential?

Yes. Only people working on the study or working to ensure the study is run correctly will have access to the data. All information collected about you during this study will be confidential and will be stored securely and not destroyed until 10 years after the study has finished.
We will tell your GP that you are taking part in this study.

What if new information becomes available?

Sometimes, during the course of a research study, new information becomes available about the drugs that are being studied. If this happens, your hospital doctor will tell you about it and discuss with you whether you want to continue in the study.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

Taking part is completely voluntary. If you decide not to take part, or if you decide to withdraw from the study after an original decision to take part, this is alright. You do not have to give a reason and it will not affect the standard of care you receive now or in the future.

If you decide to stop your treatment, you can still remain in the study, and this is what we would recommend. This means that we would still collect information about any new treatment you take, and whether you have further seizures. However, if you want to stop being in the study altogether, you can withdraw completely, and no more information will be collected about you. All information collected up until this time will be included in the study analysis, unless you request that it is not included. We will continue to communicate with your GP in the usual manner.

When people who have started in a research study withdraw from the study, it does weaken the study. Therefore, if you think it is likely that you will withdraw from the study before it finishes (which will take at least 2 years), it would be better if you do not join at the beginning. Similarly, if you are not prepared to take any medicine to stop seizures, then it would be better if you do not take part in the research study.

If you are happy with your medication, even after the study has ended, you are able to continue taking the treatment as you would in usual clinical practice.

What will happen to the results of the study?

We will publish the results of this study in a scientific medical journal. Your confidentiality will be ensured at all times, and you will not be identified in any publication. A short summary of the study and results will be provided on our website (www.epinet.co.nz).

The study data will be stored indefinitely within the on-line database (EpiNet). The data will only be removed if you withdraw your consent.

Who has reviewed this research study?

The science and ethics of this study were reviewed and approved by the Northern B Health and Disability Ethics Committee (HDEC).

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Peter Bergin, Chairman of the EpiNet study Group
Consultant Neurologist, Neurology Department, Auckland City Hospital
Phone: 09 379 7440 x 25663

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:
Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

If you require Māori cultural support, talk to your whānau in the first instance. Alternatively you may contact the administrator for He Kamaka Waiora (Māori Health Team) on:
Phone: 09 486 8324 ext 2324

- If you have any questions or complaints about the study you may contact the Auckland and Waitematā District Health Boards Maori Research Committee or Maori Research Advisor by telephoning 09 4868920 ext 3204

You can also contact the health and disability ethics committee (HDEC) that approved this study on:
Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

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Consent Form

Centre Name:

Name of Investigator:

Trial Number:|__|__|__|__|__|__|__|__|

Patient's date of birth |__|__|/|__|__|/|__|__|__|__|

If you need an INTERPRETER, please tell us.

Please tick to indicate you consent to the following		
I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.	Yes ☐	No ☐
I have been given sufficient time to consider whether or not to participate in this study.	Yes ☐	No ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐	No ☐
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐	No ☐
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes ☐	No ☐
I consent to the research staff collecting and processing my information, including information about my health.	Yes ☐	No ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I understand that there may be risks associated with the treatment if a woman becomes pregnant while taking an antiepileptic drug. I undertake to inform my partner of the risks and to take responsibility for pregnancy, and / or the prevention of pregnancy.	Yes ☐	No ☐
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes ☐	No ☐
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes ☐	No ☐
I understand the compensation provisions in case of injury during the study.	Yes ☐	No ☐
I know who to contact if I have any questions about the study in general.	Yes ☐	No ☐

I understand my responsibilities as a study participant. Yes ☐ No ☐

Declaration by participant:

I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date: