PARTICIPANT INFORMATION SHEET and CONSENT FORM

Title: EYLEA FOR THE TREATMENT OF DIABETIC MACULAR OEDEMA. (EIDEME)

Introduction

You are invited to participate in a clinical research study. This is because you have a condition called macular edema, which is caused by fluid leaking from blood vessels in your eye. This condition is a complication of your diabetes and is therefore called Diabetic Macular Edema

The study is being conducted by Dr Nitin Verma and the following ophthalmologists:

- Dr Kristin Bell
- Dr Guy Bylsma
- Dr Alex Hewitt
- Dr Andrew Jones
- Dr Andrew Traill

This document describes the study and what your role in it would be. Please take time to read the following information carefully and ask the study doctor or other study staff members to explain anything you do not understand or if you would like more information.

You may prefer to discuss the study with your friends, family or your general practitioner.

Study participation is voluntary. If you do not wish to participate you do not have to. Your doctor will provide you with the best possible care regardless of whether you decide to participate or not.

If you do decide to participate you will be asked to sign the consent section of this document.

'What is the purpose of this study?'

One method of treating the fluid in your eye is by injecting special proteins that stop the growth of leaky blood vessels and dries up the fluid in your eyes. This reduces the macular oedema and in turn may improve your eyesight.

Injections for macular oedema are often given monthly. The purpose of this study is to investigate if it is possible to get rid of the fluid and improve your vision while decreasing the frequency at which you may have injections.

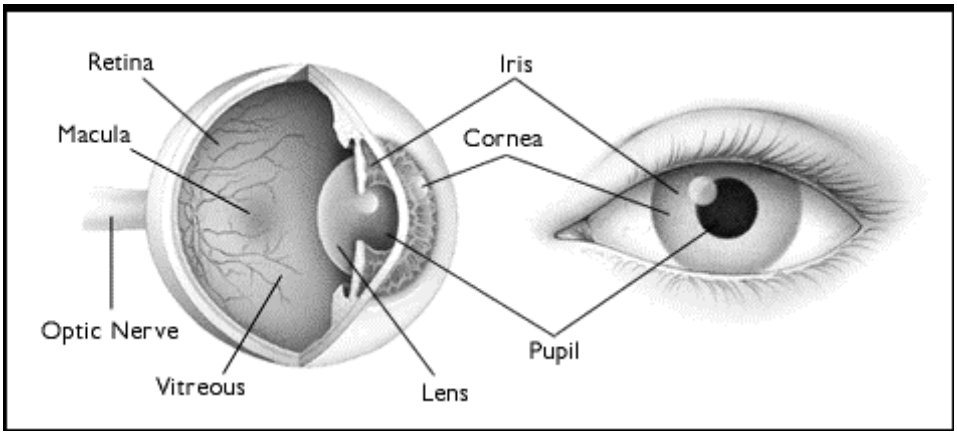
What is Diabetic Macular edema?

Your retina is the part of your eye that contains all the special light receptors that enable you to see. The macula is the part of your retina that allows you to see sharply straight ahead.

Macular oedema is observed as a complication of a number of conditions. In most cases it is caused by changes in blood vessels at the back of the eye that results in fluid leaking into the retina. This leads to accumulation of fluid and thickening of the macula. If not treated the fluid may continue to collect and may result in loss of vision and blindness.

Diabetic macular edema (DME) is a common complication of changes in the retina associated with diabetes. It is the most common cause of visual blindness in people with diabetes

The structures of the eye



In an attempt to fix the swollen retina, the walls of your retinal blood vessels leak a hormone-like factor called vascular endothelial growth factor (VEGF). This encourages the growth of new blood vessels, but unfortunately the blood vessels that grow are also leaky, and ultimately make the macular oedema worse rather than better.

'What is the study treatment?'

A number of different treatments have been used to try and control the fluid leakage including laser treatment and injection of steroids into the eye. The treatment that is currently preferred, and appears to be providing the best results in clinical trials are injections of antibody-like agents that mop up the growth factors that cause the leaky blood vessels to grow. These agents are called anti-vascular endothelial growth factor (anti-VEGF).

The treatment that will be used in this study is an anti-VEGF called Eylea.

Eylea contains the active ingredient aflibercept, which specifically recognises and binds to the VEGF and the cell receptor that it interacts with. By preventing the interaction between these Eylea may stop the growth of, and leakage from, abnormal blood vessels that cause the macular oedema. Reducing the oedema in your macula may help improve your eyesight or stop it from getting worse.

Eylea is specifically designed for injection directly into the eye

In Australia, Eylea is widely used to treat other causes of macular oedema such as age related macular degeneration (also known as wet AMD) or oedema that results from a blockage of veins in the retina. It is not yet licensed for the treatment of DEM but is already used for this condition in Europe and the USA.

The aim of this study is to investigate how much Eylea improves a patient's vision when it is given according to a patient's response to treatment rather than according to a 4 week or 8 week schedule. This is called a treat and extend regimen and is how most ophthalmologists treat patients with macular oedema in clinical practice.

'Why have I been invited to participate in this study?'

You are eligible to participate in this study because you have diabetes and your doctor has detected that you have developed macular edema and has decided that the best treatment for you at this time would be anti-VEGF injection.

'What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in this study is voluntary. It is completely up to you whether or not you participate. Whether you decide not to participate, or whether you initially participate but withdraw before the study ends it will not affect your relationship with the staff caring for you or the treatment you receive now or in the future.

'What does this study involve?'

If you decide to participate in this study, you will be asked to complete the informed consent section of this Participant Information Sheet at your next study visit..

Should you intend to participate you should also bring evidence of a recent HBC1a test to the clinic with you.

Signing the Informed Consent section acknowledges that you have read and understood this information leaflet and agree to all the procedures that are required of participants. So please ask as many questions as you need in order to make your decision whether to participate or not.

At the first study visit you will be asked for information on your medical history (including your diabetic history and control), your medications and any relevant family history of eye disease. You will also have a number of tests to assess whether you truly are eligible for the study and to establish the baseline values for your vision and retina thickness (which measured the extent of the macular oedema).

These include:

1. Measurement of your blood pressure.

2. A comprehensive eye test. For all of these tests you will be seated on a chair, and either the examiner or camera/machine will come closer to your eyes.

The eye tests include:

- Visual acuity: You will be asked to read the letters on an eye chart.
- The pressure within your eye (The intra ocular pressure) will be measured

You will then have dilating drops instilled into your eyes to enlarge the pupil. so we can look directly at the retina, optic nerve and other tissues at the back of the eye. The drops may sting and take 15-20 minutes to work. Once the dilating drops are working, you will be sensitive to light (because more light is getting into your eye) and you may notice difficulty focusing on objects up close. The effect of the eye drops may take a couple of hours to wear off.

- Scans (OCTS) and photographs of your retina:

  We will take photographs of the back of your eyes (this includes the retina and macular). To help you keep your eyes perfectly still for the photographs, you will be asked to stare at a small light. Whilst the photographer is taking the pictures, you will see a series of bright flashes.

- A Fluorescein angiogram: A special type of photograph will be taken after a special dye is injected into your arm. The dye circulates around your body and pictures are taken as the dye passes through the blood vessels in your retina. This test allows your ophthalmologist to specifically identify any leaking blood vessels.

You may already have had an angiogram before you were asked to participate in the study. If the test was done within 2 weeks of your baseline visit we will not repeat this test. The

angiogram will however be repeated at 1 year and again at 2 years at the end of the study.The study ophthalmologist will review all the above tests and will examine the back of your eye with an ophthalmoscope.

Should you meet all the criteria for inclusion in the study you will be given your first Eylea injection. For the following five months you will visit your ophthalmologist every month. From 5 months onwards the frequency of your visits will be determined by how your eye responds to treatment. There may be up to 24 clinic visits over the next 2 years

At each visit you will have your visual acuity assessed and an OCT scan of your retina taken before being examined by your ophthalmologist. Based on the results of these investigations and the clinical judgment of your ophthalmologist the time between Eylea treatments may be increased by two weeks to a maximum of 12 weeks.

By providing your consent you also give us permission to access your identified health information. This may include information from the eye clinic that you attend (The Wellington Clinic, Hobart Eye Surgeons, Tasmanian Eye Clinics or Burnie Ophthalmology), from your GP or other specialists who may be caring for you. or from your electronic records maintained by the Health Department

During the study we will keep you informed of any new information about Eylea as it becomes available, particularly if there is any new safety information that might affect your willingness to continue in the study.

If you wish to withdraw from the study at any time once the study has started you may do so without having to give a reason.

'How is this study being paid for?'

The study is being sponsored by Bayer Australia Ltd who is providing the study treatment free of charge. They have also provided some money to assist with conducting the study. All the money paid by the sponsor to assist with the running of the study will be deposited into a special research account managed by Dr Nitin Verma. It will be used to buy equipment for the study and to pay for a research assistant to help collect and manage all the information that is collected from participants.

Neither Dr Verma nor any of the other clinical investigators will personally receive any money from the sponsor.

'Are there risks to me in taking part in this study?'

All medicines may have side effects.

Some of the known side effects of Eylea are listed below. Most are not serious, but you may need medical attention if you experience some of them. Please contact your doctor if you feel unwell or believe you are experiencing a side effect of Eylea treatment.

The most commonly reported adverse effects tend to be non-serious and are short lived. These include:

- Visual disturbance, including blurred vision, dark spots or the perception that something is floating in the eye (floaters)
- Eye pain, or injection site pain
- Increased tear production (watery eyes)

Tell your doctor if you notice these. Particularly if they are worrying you.

As your vision may be blurry after dilation and injection we recommend that you DO NOT drive following your clinic visit.

Less common, more serious adverse events that have been associated with Eylea injection and should be reported to your doctor as soon as possible include:

- severe eye pain
- a sudden decrease in vision in the treated eye (possibly caused by detachment of the special retinal cells from the back of the eye).
- flashes of light or a sudden increase in floaters in your eye
- small bleeds on the surface of your eye or from the injection site
- clouding of your lens
- swelling of the eyelid or of the cornea (the clear part of your eye)
- Should you experience any signs of a heart attack or stroke (chest pain, limb numbness, slurred speech) please present to your nearest hospital emergency department immediately.

You may not experience any adverse effects, but if you do develop symptoms of any kind, listed here or otherwise, please contact your ophthalmologist or the study coordinator as soon as possible.

Are there any reasons I should not be in this study?

You should not participate in this study if any of the following applies to you:

- If you are pregnant or lactating
- If you are premenopausal (and not using contraception)
- If you have had a stroke, mini-stroke or 'heart attack' in the past 3 months.
- If you have uncontrolled high blood pressure
- If your blood sugar level is more than 12%
- If you have uncontrolled glaucoma in the study eye. (Intraocular pressure (IOP) greater than 30mmHg)
- If you are taking or planning to take medicines known to be toxic to the lens or retina or optic nerve.
- If you have any active infection or inflammation in or around your eyes
- If you have a cataract that is affecting your vision
- If you have previously received anti-VEGF injection in the study eye in the last 120 days before of screening.
- If you have had any steroid injections in the study eye in the last 6 months.
- If you have had laser treatment in the last 3 months or had more than 6 laser treatments in total.
- If you have had eye surgery in the last 2 months.
- If you have a known sensitivity to aflibercept preparations or any of its constituents. (A list of the constituents of the injection can be provided)
- If you have a known allergy to fluorescein.

PREGNANCY

As the study drug prevents the growth of new blood vessels, it is likely to damage the development of unborn babies. It is therefore very important that women participating in this study are not pregnant and do not become pregnant during the study. If you are a woman of childbearing age and there is any possibility that you are pregnant, the researchers

will need to perform a urine pregnancy test before you start in the study. If necessary, you should use reliable contraception during the course of the study. If at any time you think you may be pregnant, it is important to let your doctor know and to discontinue treatment immediately.

'What happens if I suffer injury or complications as a result of the study?'

If you suffer any injuries or complications as a result of this study, you should contact your doctor as soon as possible. Your doctor will assist you in arranging appropriate medical treatment.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is sufficiently serious and is concluded to be caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies.

You do not give up any legal rights to compensation by participating in this study.

If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.

The parties to this study agree to follow the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial. These Guidelines allow for some claims for compensation to be settled without the need for legal action to be taken. You can obtain a copy of these Guidelines from the Executive Officer of the Tasmanian Health and Medical Human Research Ethics Committee or from the study coordinator.

'Will I benefit from the study?'

This study aims to further medical knowledge and may improve future treatment of patients with diabetic macular edema, it may also benefit you. You will be receiving a treatment that has been specifically designed for treating macular edema in the eye.

'Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything. All tests and medical care will be provided to you free of charge. The study drug will be provided by the pharmaceutical company which is sponsoring the study. You will not be paid or otherwise compensated for your participation.

'How will my confidentiality be protected?'

The researchers will need to collect personal data about you which may be sensitive. (e.g. date of birth and your health information.)

Any personal or health information will be kept private and confidential. It will be stored securely and only authorised persons, who understand it must be kept confidential, will have access to it. Your study details will be de-identified with a number so that your identity will not be apparent. The research records will be kept at the Hobart Eye Surgeons and all computer files will be stored on password secured systems.

Information will only be disclosed with your permission, except as required by law. If you give us your permission by signing the Consent Form, we plan to publish the results in international scientific journals. These will not contain any identifying features.

All information collected on individual participants during the course of the study will be discussed with them at each visit and will be made available to them if requested.

'What happens with the results?'

Your individual results will be discussed with you at each consultation

The results of the study will be presented at ophthalmology conferences and will also publish as a study report in a peer-reviewed journal. When this occurs we will also provide a summary of the findings to study participants.

If necessary we may need to provide information to the sponsor or the ethics committee; particularly in relation to any adverse outcomes experienced by participants.

Information will always be presented in such a way that individual participants cannot be identified.

'What happens to my treatment when the study is finished?'

You may be able to continue Eylea following completion of this study if you and your ophthalmologist believe that you are benefiting from treatment. This decision, about the most appropriate treatment for you at that time, will be made during consultation with your treating ophthalmologist.

If you withdraw from the study, you will no longer be administered Eylea by study investigators. You will be encouraged to continue to consult with your ophthalmologist to discuss a treatment schedule that is appropriate for your needs ie withdrawing from the study will not prevent you from receiving other treatments (steroids, laser treatment or other VEGFs) as part of your routine treatment.

'What should I do if I want to discuss this study further before I decide?'

When you have read this information, your ophthalmologist will discuss it with you and answer any queries you may have while you are in clinic. If you would like to know more at any other time, please do not hesitate to contact one of the following people:

		Telephone
Principal Investigator:	Dr Nitin Verma	6210 6000
Study Coordinator:	Beverley Curry	6210 6007
OR Your study ophthalmologist at:	The Wellington Clinic (RHH)	6166 0000
	Burnie Ophthalmology	6431 7604
	Hobart Eye Surgeons	6210 6000
	Tasmanian Eye Clinic	6214 0599

'Who should I contact if I have concerns about the conduct of this study?'

This study has been approved by the Tasmanian Health and Medical Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote [HREC project number].

Thank you for taking the time to consider this study.

If you wish to take part in it, please sign the attached consent form.

This information sheet is for you to keep.