An opportunity to join a major study about diabetic eye disease in Scotland

This leaflet provides more detailed information about an important study of eye disease that can occur in people with diabetes. People across Scotland with mild to moderate diabetic eye disease are being invited to join the study and we hope that you will also consider taking part. The study could provide doctors with much better information about how to slow down, and possibly prevent, the progression of this condition in millions of people with diabetes around the world.

Please take the time to read this information leaflet before making a decision about whether or not to join this study. It is important that you know why the research is being done and what it might mean for you. Feel free to discuss this information with your family your friends and your doctor.

What is the purpose of the study?

Diabetes can affect the small blood vessels at the back of the eye, a condition called **diabetic retinopathy**. **Diabetic retinopathy** remains one of the main causes of blindness and poor vision in adults of working age, which is why NHS Scotland offers everyone with diabetes retinal screening. Retinal screening involves taking photographs of the back of the eyes (or retina) every 6 to 24 months, so that any changes caused by diabetes can be monitored. Good control of blood sugar and blood pressure reduces the chances that **diabetic retinopathy** will become severe. However, the condition is often progressive and patients may still need specialist NHS treatment such as laser therapy, surgery, or courses of injections to the eyes to preserve their vision. Each year, 5,500

patients with diabetes in Scotland need to see a NHS eye specialist because of worsening **retinopathy**. It is important therefore to find and develop simple, effective treatments that slow down or stop the progression of **retinopathy**.

The LENS (Lowering Events in Non-proliferative retinopathy in Scotland) study is investigating whether taking a drug called **fenofibrate** will slow down the progression of **diabetic retinopathy**.

Fenofibrate is a tablet that has been used to lower cholesterol for over 30 years. Two large studies have suggested that this medicine may slow down the progression of **retinopathy**. We are conducting the LENS study to find out if **fenofibrate** should be routinely used in patients with **retinopathy** to stop the condition from getting worse. Approximately 1,000 patients from across Scotland known to have diabetes and **retinopathy** will take part. With their approval, their health will be followed during the study. This will be done accurately and confidentially from a range of medical records using existing electronic systems. It will be done safely and securely in accordance with the Data Protection Act. Permission has been obtained from NHS Scotland's Public Benefits and Privacy Panel for Health and Social Care to ensure that the trial is done to the highest standards.

Why have I been invited?

Your most recent retinal screening results suggest that there is a good chance that you may be eligible to take part in the LENS trial. We are keen to offer as many people as possible the chance to take part.

Do I have to take part?

No. Participation is entirely up to you. If you agree to take part we will ask you to sign a form to record your consent. You are

free to withdraw from the study at any time, without giving a reason and this will not affect your NHS care in any way. If you choose to take part, your GP will be informed.

Who is running and who is funding the study?

LENS is being led by experienced doctors and researchers at the Universities of Oxford, Glasgow, Dundee, Edinburgh and Aberdeen. The trial is funded by the National Institute for Health Research (NIHR), which is funded by the Department of Health. The NIHR exists to improve the health of the nation through medical research. Treatment for this study has been obtained from Mylan (a pharmaceutical company), however the company plays no other role in the trial. LENS results will be analysed by researchers at the University of Oxford.

What will happen to me if I take part?

You will be asked to participate in LENS for between 3 and 5 years but will only be required to attend two face-to-face visits in a NHS research clinic at a local hospital.

Getting started

At your first visit, the study will be explained to you in more detail and you will be given plenty of opportunity to ask questions. A trained study nurse will check your medical records to ensure you meet the entry criteria to take part. If you are interested in the study and are likely to be suitable, you will be asked to sign a form agreeing to take part. The nurse will ask you about your medical history and will also take a sample of blood (you do not need to fast) to check your kidney and liver functions, cholesterol and HbA1c and, if possible, a sample of urine will also be taken. These samples will be tested in the hospital's NHS laboratory to make sure that you are suitable to take part.

You will complete two questionnaires with the nurse, one about your quality of life and the other about your eyesight. The visit will last about 60 minutes. When the research nurse receives your blood test results a few days later, you will be contacted to let you know if you are eligible to continue. If eligible, you will enter the 'run-in' phase of the study. This is an 8 week period which will allow you and the LENS doctors and nurses to be sure that you are happy to take **fenofibrate** tablets and that they agree with you. You will receive the **fenofibrate** tablets by post, along with instructions about how to take them.

After 8 weeks

After taking the **fenofibrate** tablets for about 8 weeks you will be asked to attend a second appointment (of about 45 minutes) at the same place. If you have had no problems with the study treatment during the previous few weeks, have taken them regularly and are happy to continue, you will be asked to commit to the study for at least the next 3 years. Your height, weight and blood pressure will be checked and another blood sample will be taken. A few days after the visit, once the research nurse receives these blood results, you will be contacted to confirm whether or not you are suitable to continue in the trial.

The rest of the trial

If you continue, you will receive regular supplies of study tablets by post. You will be provided with either **fenofibrate** tablets (the drug being tested) or 'dummy' placebo tablets to take for the rest of the trial. You are assigned **fenofibrate** or the dummy drug 'at random' (like the toss of a coin) which allows us to properly test whether the **fenofibrate** works. You have as much chance of receiving **fenofibrate** as you do of receiving the dummy tablet.

You will not know which treatment you receive, nor will your GP or the LENS staff. However, this information would be made available to your doctor and other medical staff if it was medically necessary. You will not need to attend the research clinic again. Study tablets will be sent to you by post every 6 months and you will be asked to complete study questionnaires over the 'phone or on your computer every 6 months.

STUDY TIMETABLE

FIRST FACE-TO-FACE APPOINTMENT (0 weeks)

Your suitability for the trial will be assessed using available information from NHS retinal screening and your medical history. You will be asked to sign a consent form. A blood test will be taken and you will be asked to complete 2 questionnaires about your quality of life and your vision.

Please remember to bring along a list of all your usual medications!

RUN-IN PHASE (0 to 8 weeks)

We will let you know your blood results from the first appointment. Assuming these are as expected, you will receive a 10 week supply of fenofibrate by post along with instructions on how to take them.

FACE-TO-FACE APPOINTMENT (8 weeks)

You will be asked whether you have had any problems taking fenofibrate. We will ask you to confirm that you are happy to take part in LENS. Your height, weight and blood pressure will be checked and a further blood sample will be taken to check your kidney and liver function.

Please bring along a list of all your usual medications again.

FOLLOW UP (3 to 5 years)

If your blood results from the second visit are fine, you will be randomly allocated to receive either **fenofibrate** or the dummy placebo tablet. You will receive a supply of tablets every 6 months by post. You will also be asked to complete questionnaires by phone or computer every 6 months. You should continue to attend NHS retinal screening as usual.

STUDY FINISHES: Results are announced*

*Participants stop the study treatment. They continue NHS follow up with their doctor.

Travel expenses

We will reimburse reasonable expenses for travelling to your LENS appointments. Please make sure you ask about this at the clinic. Taxi travel can also be provided if needed.

What will I have to do?

For LENS to produce the best results, it is important that participants stay in the study for the entire time and continue to take the study tablets as regularly as possible. The study will last at least 3 years. You can withdraw from the study at any time; alternatively, if you are worried about the study tablets, you can contact the LENS team at any time and an extra appointment can be arranged if needed. You will be asked to take either a drug called **fenofibrate** or dummy tablets (placebo) but you will not know which you are taking. This is because scientists are not yet sure whether **fenofibrate** will slow the worsening of **diabetic retinopathy** (eye disease) so they need to be sure that the results are correct and there is no bias. At the start of the study the research nurse will ask you to provide blood and urine samples for testing in your local NHS lab but the samples will not be stored. These samples will be used to check that you are suitable for the study and to ensure the **fenofibrate** is not having any adverse effects. These results will also be provided to your GP. We need about 4 teaspoons of blood on each occasion. We will also ask you to regularly complete questionnaires about your general health and about your vision during the trial.

What are the benefits of taking part in this study?

While there may be no benefit for you, you will be helping doctors and scientists improve treatment for people who have diabetes and who may be at risk of serious eye disease. If successful, results from this study will allow **fenofibrate** to be used for patients with **retinopathy** worldwide. We also know

from previous studies that **fenofibrate** may provide other benefits. For example, the medicine reduces the chance of having a heart attack by 10-15%. Your other diabetes care and any treatment you may require for **diabetic retinopathy** will not change.

Are there any risks?

Most treatments have side-effects which some people may experience and others may not. **Fenofibrate** is usually well tolerated with no serious safety problems. The 'run-in phase' will also give us a good chance to check that you have no problems with the tablets. We will send you a questionnaire every 6 months which specifically asks about your recent health. In addition, the research team will monitor your medical records regarding any admissions to hospital and any routine blood tests which you have. You can withdraw from the study at any time if you wish and this will have no impact on your usual NHS care.

Fenofibrate is already a licensed drug in the UK for treating people with raised cholesterol levels but it is not currently licensed for treating **diabetic retinopathy**. In LENS we are testing whether **fenofibrate** should be used as a treatment for patients with diabetes and **retinopathy**. **Fenofibrate** can be taken safely regardless of whether you are on a statin or not, as already confirmed in major studies. It is also safe to take with the vast majority of other medicines. We will check that you are not on any medicines which cannot be taken with **fenofibrate**. It is well known that treatment with **fenofibrate** often causes a small rise in a blood test called creatinine, which is a test of kidney function. However, creatinine then quickly returns to one's normal level when **fenofibrate** is stopped, so there is no evidence that using **fenofibrate** harms the kidney in any way.

You will receive a Treatment Information Leaflet with more details before entering the 'run-in' phase.

In large trials of **fenofibrate** and similar drugs (called fibrates), those treated with fibrates had a lower risk of suffering heart attacks and foot amputations.

If you do experience side effects, you may choose or be advised by your doctor to stop the study tablets. There is nothing to suggest that stopping the tablets will cause you any harm. If you experience unexpected symptoms after joining the study you can contact your LENS research nurse, or a study doctor on **Freephone 0808 164 5090** (available 24 hours a day, 7 days a week).

What are the other possible disadvantages of taking part?

The effects of **fenofibrate** on the unborn child and on children being breast-fed are not definitively known. For this reason **fenofibrate** should not be taken by women who are pregnant, planning to become pregnant, or breast feeding, and these women cannot take part in the study. Women who could become pregnant must use effective and reliable contraception during the study and for 7 days after the end of the study (i.e. after stopping study treatment). If you become pregnant during the trial (or plan to become pregnant), you should tell your research nurse or the LENS trial doctors immediately so appropriate steps can been discussed.

What happens when the study stops?

Once the study is over you will no longer be provided with the study treatment. You and your doctor will be informed of the results which will also be published in a medical journal, so that others can benefit from the research. If the trial proves that **fenofibrate** does reduce **diabetic retinopathy**, it is likely that

this information will be included in major guidelines which doctors use to treat diabetes. That will allow many people with diabetes to be offered **fenofibrate**.

After the trial ends, we would also like your permission to continue to monitor your health confidentially from a range of medical records using existing electronic systems in the same way that we will be doing during the trial. This is to allow the LENS researchers to study the effect of 3-5 years of **fenofibrate** treatment for many years to come. Permission will be required from NHS Scotland's Public Benefits and Privacy Panel for Health and Social Care before any such work is undertaken to ensure that it is done to the highest standards and in accordance with the Data Protection Act.

What if there is a problem?

If you have any concerns about any possible side-effects of treatment or any complaints about the way you have been dealt with in the study, please call the study team on **Freephone 0808 164 5090**. More detailed information is given in Part 2.

Part 2: Further details for patients who want them

What if relevant new information becomes available?

Sometimes, during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the research team will tell you about it and discuss whether you want to, or should, continue in the study. If you decide not to carry on, your research nurse will make the necessary arrangements. Upon receiving new information, your own doctor might consider it to be in your best interests to stop the study treatments. They will explain the reasons if this needs to happen. If the study is stopped for any other reason, you will be told why.

What if I don't want to carry on with the study?

If you wish to discontinue your study treatment we would advise you to do this in consultation with the LENS research team. However we'd still like to send you questionnaires to ensure the study's results are reliable. You are free to completely withdraw from the study at any time in which case you will not receive any further questionnaires.

For women: Women who could become pregnant must continue to use effective methods of contraception for 7 days after stopping study treatment (or the end of the study).

What if there is a problem?

You retain all the usual rights of a NHS patient. The University of Oxford, which is sponsoring the trial, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in the trial. If you have a concern about any aspect of the study you can speak with the LENS researchers. They can be contacted on a 24-hour Freephone number: **0808 164 5090** or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224 or the head of CTRG, email ctrg@admin.ox.ac.uk. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the Patient Advice and Support Service (however, this service is unable to provide information about this study) at: http://www.patientadvicescotland.org.uk/

Will my taking part be kept confidential?

Yes, absolutely. If you accept this invitation, your contact details will be stored securely so that further information can be sent to you (these details can only be seen by your local research team and by staff working in the co-ordinating centres at the

Universities of Oxford and Glasgow). The central co-ordinating centre in Oxford will seek information from NHS and other central registries about any serious illnesses, retinal screening results and blood results taken as part of your usual care. The central co-ordinating centre may also contact your doctor if any further information is required. For these reasons we require your name, date of birth and CHI number (your unique number in the NHS). All information obtained will be kept confidentially and only used for medical research. PCI Pharma Services are responsible for mailing study medication. To do so they require temporary access to your name and address – this will be provided securely by Oxford. Your personal details will never be transferred to any other party. Responsible members of the University of Oxford, your host NHS health board, or regulatory authorities may be given access to data for monitoring and/or audit of the study to ensure compliance with regulations. Information used for scientific analyses will never include any details that identify you.

What will happen to the results of the research study?

It is intended to present the results at a major medical conference and publish them in an appropriate medical journal. No patient will be individually identified in any report or publication.

How is this study organised?

Scientists and doctors consider the question being asked by LENS important because it could improve treatment for people who have diabetes by reducing the risk which **retinopathy** poses to vision. The study design has been reviewed and agreed by the West of Scotland Research Ethics Committee whose duty it is to check whether the health question being asked is important enough to warrant a study, and that the

study is being carried out in an independent, honest and professional manner. Scientists at the University of Oxford are co-ordinating the study with the collaboration of the Universities of Glasgow, Aberdeen, Edinburgh and Dundee, and with doctors and nurses from around Scotland.

An independent committee oversees the study and monitors the results. This committee could stop the study early if important new evidence emerged that had an impact on the need for the study to continue.

Thank you for your interest in this study. Our aim is to make your participation an interesting and worthwhile experience, while helping us and others to improve the treatment of people who have **diabetic retinopathy**.

General Data Protection Regulation and LENS Trial

The **General Data Protection Regulation** is a European Union regulation which came into force on 25th May 2018 and concerns individual privacy and data protection. To comply with this regulation we are required to provide the following information to all LENS trial participants. If you agree to take part, the following will apply:

- The University of Oxford is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this trial. This means that we are responsible for looking after your information and using it properly. The University of Oxford will keep identifiable information about you for a maximum of 10 years after the trial has finished.

- Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information by contacting the Chief Investigator, David Preiss, at lens@ndph.ox.ac.uk.

- The University of Oxford and your NHS health board will use your name, CHI number and contact details to contact you about the research trial, and make sure that relevant information about the trial is recorded for your care, and to oversee the quality of the trial. Individuals from the University of Oxford and regulatory organisations may look at your medical

and research records to check the accuracy of the research study. Your NHS health board will pass these details to the University of Oxford along with the information collected from you and/or your medical records. The only people in the University of Oxford who will have access to information that identifies you will be people who need to contact you by ‘phone, arrange sending you letters and postal questionnaires, arrange posting of study medication, or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, CHI number or contact details.

- Your health board will keep identifiable information about you from the trial for a maximum of 10 years after the trial has finished.

- When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

- Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

- Where this information could identify you, the information will be held securely with strict arrangements about who can

access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

- Where there is a risk that you can be identified, your data will only be used in research that has been independently reviewed by an ethics committee.

Questions about the study should be directed to the co-ordinating centre in Oxford.

By 'phone:

24-hour Freephone service: **0808 164 5090**

By post:

LENS trial, CTSU, Richard Doll Building, University of Oxford, Roosevelt Drive, OXFORD, OX3 7LF

By email:

lens@ndph.ox.ac.uk

Or visit our website:

www.ctsu.ox.ac.uk/lens