Participant Information Sheet

A Randomised Controlled Trial Of Nortriptyline In Knee Osteoarthritis

Ethics committee ref.: **14/NTA/139**

INTRODUCTION

You are invited to take part in a study on a treatment for osteoarthritis knee pain. It is your choice whether or not you take part. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you decide to take part, but change your mind later, you can withdraw from the study at any time. We are unable to provide an interpreter for this study.

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 happens after the study ends.

We will discuss 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 like to discuss the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

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.

This document is six (6) pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

Osteoarthritis (OA) is common and painful. The painkiller medicines currently available for OA pain are not perfect: they are either not very effective or cause unpleasant or dangerous side effects. Recent research has shown how the brain processes pain in OA. This research has opened up the possibility of using different types of medicines for OA pain. Nortriptyline has been used to treat pain in other conditions, and similar medicines may reduce pain in knee OA. It is not known whether nortriptyline is useful in this condition. We plan to test this by giving people with knee OA either nortriptyline or placebo and to measure changes in pain before and after a period on the medication.

Our aim is to test the effect of nortriptyline taken in addition to participants' usual pain relieving treatments. Participants will continue to take their other medications as usual during the study. The study is funded by a grant from the Health Research Council of New Zealand. The researchers are based at the University of Otago, Christchurch and the Canterbury District Health Board (CDHB). Contact details for the lead investigator of the study can be found at the end of the information sheet. The study has ethical approval from the Northern A Health and Disability Ethics Committee.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

You have been invited to take part in the study as you have been identified by the Canterbury District Health Board (CDHB) Orthopaedic Outpatient Department or by your GP as having OA affecting one (or both) of your knees, or you have contacted us yourself. If you decide to participate in the study you will be asked to take study medication in addition to your usual treatments for 14 to 17 weeks. The study medication may be the active medication nortriptyline or an identical placebo. Neither you nor the researchers will know which medication you will receive until the study is finished.

If you choose to take part you will be asked to attend a clinic appointment with the research nurse to check you are eligible for the study. This appointment will be in Christchurch and will take approximately 45 minutes. If you are eligible to participate you will be asked to attend another study clinic appointment (which will also last about 45 minutes) during which you will be asked questions about your knee pain and how it affects you. At this visit we will give you a supply of study medication. The study takes 14 to 17 weeks altogether. The research nurse will phone you every 2 weeks for the first 8 weeks of the study to adjust the dose of the study medicine. You will then continue taking the study medicine at a steady dose for another 6 weeks. At the end of the study you will attend a final study clinic appointment with the research nurse to measure your pain, function, quality of life and medication side effects.

Sometimes when nortriptyline is stopped after using it for a period of time, withdrawal symptoms may occur (for example chills, headaches, muscle pain, nausea and insomnia). Treatment is not required for these symptoms and they usually do not last long. The chance of having withdrawal symptoms is reduced if the dose is slowly reduced. Participants will therefore be asked to reduce their daily dose by 1 capsule every week until they have stopped altogether. For example, if your final dose was 3 capsules daily then after the study period has finished you would take 2 capsules daily for 1 week, then 1 capsule daily for 1 week and then stop.

When you have finished taking part in the study we will write to you and your GP to let you know whether you took the active treatment or a placebo during the study. If you had taken the active treatment during the study and found it useful you could then discuss whether to continue it with your GP.

Information gathered about you for this research will be recorded and stored in a secure filing system and in a password-protected database.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

If our hypothesis is correct, participants who take nortriptyline will experience less pain from their knee arthritis. Nortriptyline has been widely used for many years and, like all medications, it can cause side effects and the following are common or important:

- dry mouth
- blurred vision
- constipation
- urinary retention
- irritability
- sleep disturbances
- drowsiness
- agitation and/or confusion
- anxiety
- sexual dysfunction
- dizziness

Nortriptyline must be used with caution in patients with heart disease (e.g. angina or a previous heart attack) because it may increase the risk of heart rhythm irregularities, heart attacks and strokes.

To reduce the risk of adverse effects, the medication will be started at a low dose. The dose will be altered every two weeks according to your response. If you choose to take part you will be free to stop taking the study medication at any time during the study.

We will inform your GP about your involvement in the study. Your usual medical care will continue to be provided by your GP. The researchers will not be involved with this.

WHO PAYS FOR THE STUDY?

The study is fully funded by the Health Research Council of New Zealand. Participants will not incur any costs. We will provide $10 fuel vouchers to participants to compensate them for the cost of attending each study clinic appointment.

WHAT IF SOMETHING GOES WRONG?

If you were injured in 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, which may take some time to assess. 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.

WHAT ARE MY RIGHTS?

It is your choice to take part in the study. If you decide to take part you are free to withdraw from the study at any time – this would not affect your usual medical care in any way. If you do take part in the study you have the right to access information which will be collected about you. You will be told about any important new information about the benefits or harms of the treatment that becomes available during the study.

Study interviews will be conducted in confidence and all information about you will be stored in a secure filing system and a secure database. Research material is held for a minimum of 10 years after completion of the study and is the responsibility of the principal investigator. All information is confidential and no material that could personally identify you will be used in reports or publications resulting from the study.

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

At the end of the study period, you and your GP will be told whether the study medication you took was nortriptyline or placebo. If you wish to continue taking nortriptyline after the study period, you will need to consult your GP. You would be responsible for the cost of this consultation and of any ongoing prescriptions.

Once the study is complete and we have analysed the results, we will prepare a summary of the main findings. This will be sent to participants who indicate they would like to receive it. We expect that this information will be available by the end of 2017.

WHAT ARE THE POTENTIAL HARMS IF I BECOME PREGNANT DURING THE STUDY?

Nortriptyline has been used by pregnant women for many years and is considered to be relatively safe. Some studies have, however, shown that nortriptyline may increase the risks of foetal abnormalities and of pre-term delivery. Newborn babies whose mothers took nortriptyline in pregnancy may experience withdrawal symptoms.

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 the study's principal investigator:

Dr Ben Hudson
Principal Investigator
Department of General Practice
University of Otago, Christchurch
Phone: 03 364 3607
Email: ben.hudson@otago.ac.nz

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

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