[INSERT LOCAL DEPT/INSTITUTION DETAILS HERE]

Allopurinol and cardiovascular outcomes in patients with ischaemic heart disease (**ALL-HEART)**

CONTACT DETAILS:

If you are interested in taking part in the ALL-HEART study, or would like to ask any questions about the study and what it involves, please contact the local study doctor or one of our research nurses, who would be happy to answer any questions.

Name: **[INSERT LOCAL INVESTIGATOR HERE]**
Position: **[INSERT STUDY POSITION HERE]**
Telephone: **[INSERT LOCAL TELEPHONE HERE]**
Freephone: 0800 7310243
E-mail: **[INSERT LOCAL CONTACT EMAIL HERE]**
Address: **[INSERT LOCAL CONTACT DETAILS HERE]**

PARTICIPANT INFORMATION SHEET:

We would like to invite you to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve for you. One of the research team will go through the information sheet with you and answer any questions you have. You will be given as much time as you need to consider whether or not you wish to take part. This participant information sheet is split into 2 parts:

Part 1 tells you the purpose of the study and what will happen to you if you take part.
Part 2 gives more detailed information about the conduct of the study.

Please take the time to read this information carefully. You should talk to the study doctors or nurses about this study and ask any questions you have. You can also discuss this study with other people such as your family or your family doctor (GP). If you decide to participate in this study, you will be asked to sign and date a consent form. You will receive a copy of the signed form.

PART 1: What is the purpose of the study and what will happen to me if I take part?

What is the purpose of this research?

We are doing this research because we want to improve the treatment of patients with ischaemic heart disease (IHD). IHD is a common problem in the UK, involving narrowing or partial blockage of the blood vessels to the heart. It can sometimes result in chest pain (angina) or even heart attack (myocardial infarction). The ALL-HEART study will investigate whether there is any benefit to patients with IHD of taking a tablet called allopurinol. The kind of benefits we are looking for include improved symptoms and a reduced risk of things like heart attack, stroke and other health problems occurring in the future. It will also investigate whether allopurinol therapy improves quality of life in patients with IHD and whether allopurinol is a cost-effective medicine for the NHS to give to patients with IHD by looking at whether allopurinol reduces the number of hospital admissions due to cardiovascular problems and whether it reduces the number of visits patients make to their GP, nurse or outpatient clinics.

Allopurinol is a well established and widely prescribed medicine that has been used for more than 50 years to prevent gout attacks in patients with gout. It is not currently used as a specific treatment for IHD (although many patients with IHD will have taken it to prevent gout). Recent research suggests that allopurinol may also have positive effects on the cardiovascular system (the heart and blood vessels). For example, there is some evidence that it may improve blood pressure, improve endothelial function (the way the lining of the blood vessels works) and reduce thickening of the heart muscle. Allopurinol may also increase the time patients with angina can exercise before they get chest pain. We now want to study whether it can lead to even greater benefits (such as reduced risk of heart attack, stroke or even death due to cardiovascular disease) and to do this we need to do a larger study in thousands of patients with IHD. We do not currently know whether or not it will have benefit for such patients and that is why we are doing this study. The ALL-HEART study will include 5,215 patients with IHD and will last for around 5 years. It will include patients in Scotland and England.

Why have I been invited?

You have been invited because we think you may have a history of IHD (angina or heart attack) at some time (although you may or may not currently have any symptoms). Your doctor has agreed that we may write to you and invite you to take part.

Do I have to take part?

Taking part in medical research in the UK is entirely voluntary and you should feel under no pressure to take part if you do not think it is right for you.

If you are interested in finding out more about the study a member of the study team will contact you to discuss the study and what it involves. You can then make an informed decision on whether or not you wish to take part.

You are free to withdraw from the study at any time without giving a reason. If you decide not to take part or change your mind at any time, this will not affect your current or future care in the NHS.

What will happen to me if I take part?

If you are interested in taking part in the ALL-HEART study, we will arrange an appointment with a nurse, usually at your own GP practice. This appointment should take around one hour. The nurse will discuss the study with you and answer any questions you may have. If you decide that you would like to take part, you will be asked to sign a consent form. The nurse will then ask you some questions about your medical history, current health and the medicines you take. You will have your blood pressure, pulse rate, weight and height measured and we will take a blood sample (around 10ml in total) to check your full blood count, kidney function and urate level. You will be asked to complete two short questionnaires about your condition and how it affects your quality of life. The nurse will also review your medical records to check that you are eligible to take part in the study and that it is likely to be safe for you to do so.
Sometimes we don't know which way of treating patients is best. To find out, we need to make comparisons between different treatments. We put people into groups and give each group a different treatment. Each patient is put into

a group by chance (randomly). The results are then compared between the groups. In the ALL-HEART study, one group of patients will receive allopurinol therapy in addition to their usual treatment and the other group of patients will not receive allopurinol but will continue to receive their usual care for their IHD. You will have a 50:50 chance of receiving allopurinol in addition to your usual treatment or of receiving no additional treatment in addition to your usual treatment. You should only take part in the study if you are willing to accept the chance of being randomly allocated to either group. Because the groups of patients in the study are allocated by chance you cannot choose which group you would like to be in and the nurse cannot choose this either.

Patients allocated to receive allopurinol:

If you are randomly allocated to the group of patients to be given allopurinol, the nurse will contact you, usually by telephone, once your blood results have been checked. Provided your blood results are satisfactory, the nurse will arrange for a prescription for allopurinol to be issued and will let you know when you can collect it. You can then start taking the allopurinol according to the dosing instructions. One of the blood tests we check is your kidney function. The maximum dose of allopurinol we give you in the study will depend on whether one part of your kidney function test (the 'eGFR') is normal (60 ml/min or greater) or reduced (between 30 and 59 ml/min) when the nurse checks your blood test result. The nurse will explain this to you when she telephones you.

For patients with a normal kidney function test, the dose of allopurinol will increase gradually over 6 weeks so that you are given 100mg daily for the first two weeks, then 300mg daily for two weeks, then 600mg daily thereafter. You will then keep taking the allopurinol at 600mg daily for the duration of the study (up to 5 years) unless you have any side effects or decide that you want to stop taking it.

For patients with a reduced kidney function test, the dose of allopurinol will increase gradually over 4 weeks so that you are given 100mg daily for the first two weeks, then 300mg daily thereafter. You will then keep taking the

allopurinol at 300mg daily for the duration of the study (up to 5 years) unless you have any side effects or decide that you want to stop taking it.

You should continue with your other medications as normal throughout the trial unless your doctor advises you otherwise.

If you are given allopurinol, a second visit with the nurse will be arranged around 6 weeks after your first visit. At this visit, the nurse will check whether you have had any side effects with the allopurinol and will take another blood sample (10ml in total) to check your full blood count, kidney function and urate level. This visit should only take about 15 minutes.

Patients allocated to receive no additional therapy:
If you are not allocated to the group of patients to be given allopurinol, you will have no further study visits with the nurse.

All patients:
All patients (whether given allopurinol or not) will be contacted again 1 year after starting the study. You will be asked to complete the two questionnaires again about your quality of life (the same ones that you completed at your first visit with the nurse) and will be asked some questions about how many times you have visited your GP, your practice nurse, physiotherapist and any hospital outpatient clinics in the last year. We will also ask you if you have had any specific problems that are sometimes related to allopurinol therapy such as any gout attacks or rashes. To make this as easy as possible for you, these questionnaires can either be answered electronically if you use the internet, or by completing a paper version and returning it to us by post or by telephone. We will ask you which way you would prefer.

For patients taking allopurinol, we will also ask you to tell us if you have had any other side effects and ask you to confirm whether you are still taking the allopurinol. We will do this once a year for the duration of the study (up to 5 years).

At the end of the study, we will ask you to complete the quality of life questionnaires again and tell us how many times you have visited your GP, practice nurse, physiotherapist and any hospital outpatient clinics in the last year. In addition, 25% of patients will be contacted at years 2, 3 and 4 and asked about how many visits to their GP, practice nurse, physiotherapist and outpatient clinics they have made in the last year.

No other visits to your GP or hospital are needed as part of the study.

Every year, we will receive information from centralised electronic NHS databases in Scotland and England for all patients taking part in the ALL-HEART study. This information will include details of any hospital admissions that have occurred during the year and may include sensitive details, for example, about any admissions for mental health conditions. This process is called record-linkage. It allows us to follow up how many patients have had major problems such as heart attacks, strokes or heart failure, and other important healthcare events. We will also receive information from centralised electronic databases in Scotland and England on any deaths that have occurred in patients who are taking part in the study. In Scotland this information comes from the Information Services Division (ISD) and in England it comes from the Health and Social Care Information Centre (HSCIC), known as NHS Digital. HSCIC was established in April 2013 and is responsible for providing a trusted safe haven for some of an individual's most sensitive health and social care information. NHS Digital collects information from the records health and social care providers keep about the care and treatment they give. The data is collected from a wide range of providers across England ranging from hospitals to general practices. One of the datasets collected is called Hospital Episode Statistics (HES). This is information about patients in relation to their NHS visits and stays at hospitals in England. The information collected contains details of admissions to hospital, outpatient appointments, and A+E attendances.
For us to follow you up through record linkage we need to tell ISD Scotland (if you live in Scotland) or NHS Digital (if you live in England) who you are, so that they can supply your records to us. We will supply a list of individuals' details

(NHS number (or Community Health Index (CHI) number in Scotland), date of birth, postcode and gender), and they will return your hospital and mortality records to us identified by your ALL-HEART study participant number. All transfer of data is handled securely, in line with NHS standards.

What will I have to do?

The study medication should be taken as prescribed and we would like you to inform your GP or research nurse about any problems during the study. If you experience a problem that could be a side effect of the study drugs or if you are hospitalised or have to see a doctor in an emergency whilst you are outside the United Kingdom you should also tell your GP or research nurse. If you stop taking allopurinol for any reason while you are taking part in the study please contact the research team to let them know.

What will happen to any blood samples I give?

The blood samples you give will be tested by a local NHS laboratory to make sure that it is safe for you to take part or continue to take part in the ALL-HEART study and the results will be sent to your GP and checked by the study nurse. Any remaining blood will be destroyed within a few days of the laboratory test being completed. No samples will be stored for future use.

What is the drug that is being tested?

Allopurinol is the drug that we are testing in this study. It is licensed in the UK for the prevention of gout. It is not currently licensed for use to treat IHD, although many patients with IHD will have taken it for other reasons. In this study, allopurinol will be taken orally as a tablet. In patients with normal kidney function tests at the first study visit, it will be started at low dose of 100mg daily then increased after 2 weeks to 300mg daily, then increased after 2 more weeks to 600mg daily. It will then be taken at 600mg daily for the rest of the duration of the study (up to 5 years). In patients with reduced kidney function tests at the first study visit, it will be started at low dose of 100mg daily then increased after 2 weeks to 300mg daily. It will then be taken at 300mg daily for the rest of the duration of the study (up to 5 years).

What are the possible disadvantages and risks in taking part?

Blood sampling may cause minor discomfort and bruising. If during the course of this study, we discover any previously undiagnosed health problems then you and your GP will be notified.

What are the possible side effects of allopurinol?

Allopurinol is a well established and widely prescribed drug, but like all drugs it has a number of potential side effects. Known possible side effects include skin rash. This affects around 1 in 100 people and can occasionally be serious (in about 1 in 1000 to 1 in 10,000 people). Other possible side effects include nausea, vomiting, drowsiness, allergic reactions and diarrhoea. In patients who have undiagnosed gout, starting allopurinol may potentially trigger an acute attack of gout (pain in a joint, usually the big toe). If you experience any other side effects or symptoms you think may be related to you taking allopurinol you should contact the research team or your GP for further advice.

If you develop a new skin rash or an allergic reaction after starting to take allopurinol you should stop taking it immediately and contact the research doctor, research nurse or your own GP for further advice.

What are the alternatives for treatment?

If you do not want to take part in the ALL-HEART study, your family doctor will continue to give you the usual care for patients with IHD.

What are the possible benefits of taking part?

Until we complete this study, we do not know whether allopurinol will have benefits for patients with IHD. Taking part in the ALL-HEART study may not result in any benefit to you personally but every person is different and the information we get may help to improve the treatment of people with IHD in the future. The study doctors and nurses can answer any questions you may have about which tests and procedures are not part of your usual medical care.

How long will I be involved in the study?

We expect the study to run until the end of 2018. Depending on when you join the study, you may be involved in the study for up to 5 years. During this time

we will contact you once a year (or more often if you have any problems) and we will also let you know when the study has finished.

What happens when the study stops?

When the study finishes you will no longer be prescribed allopurinol by your GP. Your GP will continue to give you the usual care for patients with IHD. Your study doctor will let you know the results of the study after the study has finished.

Will my expenses be reimbursed?

Reasonable travel costs, such as bus fares or a mileage rate of 45 pence per mile travelled, plus parking when using a personal vehicle, will be paid for visits which are directly related to participation in the study.

What if there is a problem?

If you have a complaint about your participation in this study, you should first talk to a researcher involved in your care or your GP. You can ask to speak to a senior member of the research team or the Complaints Officer for NHS**[INSERT LOCAL HEALTH BOARD/CCG HERE]**. In the unlikely event that something goes wrong and you are harmed during the study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for legal action against either the University of Dundee or NHS Tayside or your GP. Please contact your GP practice for details on how to register a complaint.

The normal National Health Service complaints mechanisms will still be available to you.

[INSERT LOCAL NHS COMPLAINTS SERVICE DETAILS HERE]

This completes Part 1 of the information sheet. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART 2: More detailed information about the study

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

You can withdraw from the study at any time. If you stop study treatment we will ask you if you are happy to continue with the annual follow up questionnaires, as this information is still useful to the study. You are also free to withdraw your consent completely in which case we would not contact you or access your medical records again.

How can I withdraw my consent?

If you would like to withdraw your consent from the ALL-HEART study, you can contact the ALL-HEART study team on 0800 7310243 or 01382 383119. You can also withdraw your consent by writing to us at The ALL-HEART study, Medicines Monitoring Unit (MEMO), Mailbox 2, Level 7, Ninewells Hospital and Medical School, Dundee, UK, DD1 9SY or by sending an email to allheartreplies@memo.dundee.ac.uk. If you withdraw consent, you will not be asked to provide further details.

What if relevant new information becomes available?

Sometimes during the course of a research project new information becomes available that may affect your continuing participation in the study. If this happens, your GP or one of the study doctors or nurses will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your GP will continue to give you the usual care for patients with IHD. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your study doctor might consider it to be in your best interests to withdraw you from the study. They will explain the reasons and arrange for your care to continue.

What will happen to my data?

This study is led by The University of Dundee. The University of Dundee works with the Robertson Centre for Biostatistics, University of Glasgow on the ALL-HEART study. The Robertson Centre is an ISO27001 (security certificate) approved academic unit within the University of Glasgow that has a lot of experience in handling patient data for clinical trials and undergoes regular audits and inspections. The data relating to the ALL-HEART study will be stored and analysed at the University of Glasgow, under the control of the University of Dundee, as an academic collaboration that was approved when the grant to perform the ALL-HEART study was awarded by the National Institute for Health Research (NIHR). This collaboration is described in the study protocol and has been included in all relevant approvals, such as ethics.
The data collected with regard to you taking part in this study will be stored for a minimum of 5 or 15 years following the end of the study, depending on whether the results of the study suggest that we should introduce allopurinol as a routine treatment for IHD.

Will my taking part in the study be kept confidential?
Yes, information about your taking part in the study will be kept confidential.
If you agree to take part in the ALL-HEART study, approved members of the study team will be able to access your medical records where it is relevant to you taking part in this study. It is a requirement that relevant sections of your medical notes and research data may be looked at by responsible individuals from research regulatory authorities, the NHS or monitors appointed by the study sponsors (University of Dundee and NHS Tayside) to check that the research is properly conducted and the interests of those taking part are adequately protected.

Information obtained from you for the purpose of this research will be entered into a secure database and will be associated with you only by using a participant identification number, your date of birth, and your gender. Only the study doctor and their research staff and approved data management staff at The Robertson Centre for Biostatistics, University of Glasgow will be able to link your identification number to you. Your completed consent form for this study will be scanned and an electronic copy will be stored on a separate secure

database held at The Robertson Centre for Biostatistics, University of Glasgow. Any information collected as part of your standard clinical care will be stored on secure NHS systems.

Your participation in this study will be noted in your medical records and with your consent your GP will be informed that you are taking part in this study.

You should be aware that if you apply for health insurance you may be asked questions about your health, including your medical history and pre-existing medical conditions, even if those are diagnosed as part of a clinical research trial. The insurer may take this into consideration when deciding whether to offer insurance to you.

What will happen to the results at the end of the study?

It is likely that a report containing the results of this study will be written, presented at scientific meetings and published in scientific magazines following the end of the study. This will help doctors and the NHS to decide if allopurinol is beneficial in the treatment of patients with IHD. The data will be anonymised and no individual will be identified in any study reports.

Who is organising and funding the research?

The Medicines Monitoring Unit (MEMO) at The University of Dundee is organising this study and the study is funded by the National Institute for Health Research, Health Technology Assessment Programme (www.nihr.ac.uk). No member of the research team is being directly paid for including you in the study.

Who has reviewed the study?

The East of Scotland Research Ethics Committee REC2, which has responsibility for scrutinising all proposals for medical research on humans in Tayside, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant records, be made available for scrutiny by monitors from the University of Dundee and NHS Tayside, whose role is to check that

research is properly conducted and the interests of those taking part are adequately protected.

You will be given a copy of this Patient Information Sheet and a copy of the signed Informed Consent Form to keep if you decide to take part.

Who should I talk to if I have any further questions?

Now or during the course of the study, if you have any questions concerning this study, please contact:

[INSERT LOCAL CONTACT HERE]

In the event of a medical emergency, please contact NHS 24 on 111

Thank you for taking the time to read this information sheet and for considering taking part in this study.