Newcastle University

CONFORM-OH

Trust headed paper

Patient Information Leaflet

CONFORM- OH

Control, **F**ludrocor**t**isone **o**r **M**idodrine for the treatment of **O**rthostatic **H**ypotension

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You have been given this information leaflet because you are receiving treatment for or have been diagnosed with Orthostatic Hypotension and **may** be eligible to take part in a research trial.

Taking part in the trial is voluntary but before you decide whether to take part, it is important that you understand why the research is being carried out and what it would involve for you.

Please take the time to read through the following information and ask us if you have any questions or would like more information.

What is the purpose of the study?

Orthostatic hypotension (OH) (also called postural hypotension) is a condition where a person's blood pressure drops abnormally low when they stand up after sitting or lying down. Not everyone who has this condition has symptoms, but it can lead to dizziness, headaches, tiredness, fainting and falls.

Initial treatment is usually with non-drug therapies, including education, lifestyle advice and medication review (also called conservative treatment). Patients may also be taught leg muscle squeezing exercises and may be prescribed compression stockings. If symptoms do not improve with education and lifestyle advice, then medications to treat OH may be considered.

Two medications that are commonly used in the NHS to treat OH are Fludrocortisone and Midodrine. Fludrocortisone is a type of steroid that is used to raise blood pressure by increasing sodium (salt) levels, and Midodrine has a direct effect on the blood vessels to raise blood pressure.

Conservative treatment, Fludrocortisone and Midodrine are routinely used to treat OH in the NHS, but we do not know which one is most effective at improving the symptoms of OH.

The purpose of this trial is to find out which of these treatments are more effective at improving the symptoms of OH.

What are we doing?

We are carrying out a research trial to compare the effects of three different treatment regimens on the symptoms of OH. We will recruit 366 patients from up to 20 hospitals around the UK. Each of the participants will receive one of the following three treatments:

1. Conservative treatment only
2. Conservative treatment plus Fludrocortisone
3. Conservative treatment plus Midodrine

We will monitor the effect on patients' blood pressure and symptoms as well as any side effects from the medications to find out if any of the treatments are more effective at improving the symptoms of OH. We will also look at how much each treatment costs.

What happens next?

- If you were provided this Patient Information Leaflet before your routine clinical appointment your doctor will discuss the trial with you and let you know if you are eligible to take part at your next appointment. You will be given the opportunity to ask any questions at your appointment.

- If your doctor gave you this Patient Information Leaflet at your routine appointment they will have discussed if you are eligible to take part. With your permission your doctor or a member of the study team will contact you again to discuss the trial and answer any questions.

Do I have to take part?

No, it is up to you to decide if you want to take part in this trial. If you decide not to take part this will not affect the routine care you will receive. If you decide to take part, you can change your mind and withdraw from the study at any time and this will not affect the routine care you will receive. If you decide not to take part, or withdraw from the study you do not have to give a reason, however, we would like to know your reason if you are happy to provide this information.

What would taking part involve?

If you decide to participate in the research trial you will be asked to sign a consent form and with your consent, we will send a letter to your GP to inform them that you are taking part in this trial. You will then be asked to complete some questionnaires about your symptoms, quality of life and your ability to carry out daily activities. If you have Parkinson's disease you will be asked to complete an additional questionnaire relating to the symptoms you experience. A lying and standing blood pressure assessment will also be carried out where possible.

To reduce any additional burden or inconvenience, every effort will be made to carry out all research activity at the same time as your routine clinical appointments. These

may take place in person at outpatient clinics, by video consultation or over the phone depending on your hospital's local policy.

When these assessments are completed you will be allocated to one of the three treatment groups. You will have an equal chance of being allocated to each group.

1. Conservative management

Patients in the conservative management group will continue with non-drug treatments. This will usually include education about OH, lifestyle advice to help with symptoms, medication adjustments, water, salt and dietary advice, muscle squeezing exercises, and the provision of compression garments. This advice will vary between individuals as your doctor will provide the ones most appropriate to you.

2. Conservative treatment plus Fludrocortisone

In addition to the conservative treatment you will receive fludrocortisone which is taken orally.

3. Conservative treatment plus Midodrine

In addition to the conservative treatment you will receive midodrine which is taken orally.

You will be provided with a falls diary to complete at home for the 12 months you are taking part in the study, here you will be asked to record any falls or faints you have where you landed on the floor, ground or lower level. A faint is when you pass out (sometimes called "blacking out" or losing consciousness) for a short time due to low blood pressure. A fall is where you fall to the ground for any reason, such as losing your balance, but do not faint or lose consciousness.

3, 6 and 12 month visits:

During your study participation you will take part in three follow up visits. The following activities will take place at each visit:

- Your doctor will review of your OH symptoms
- Lying and standing blood pressure (either at a face to face appointment or may be arranged for you to take at home) and a list of your current medication will be collected.
- Your doctor will review of your treatment, which may include changing the dose of your medication.
- You will complete three self-reported questionnaires in relation to your quality of life and your ability to carry out daily activities and a review of your falls diary.

A member of the research team will contact you to arrange these visits to be at the same time as your usual clinic appointment. Visits will be conducted in clinic, at your home or over the phone (this will differ depending on your hospitals policies).

If your clinic appointments are carried out remotely you will need to provide self-recorded blood pressure measurements, using your own blood pressure machine or one provided by the study. You will be provided with instructions to help you to do this.

What are the side effects if I receive medication as part of the study?

As with any medicine, the medications used in this study may cause side effects. These include:

Fludrocortisone: swelling of the ankles, nausea, headaches, insomnia (this may be avoided by taking the medication in the morning), mood changes, low potassium levels in the blood, and high blood pressure.

Midodrine: goose bumps, headaches, flushing, feeling sick, tingling skin, high blood pressure, and difficulty passing urine.

If you experience any of these side effects it is important that you let your doctor know. The study doctor can talk to you more about what these mean if you are unsure about any of them.

What are the possible risks and benefits of taking part?

We think there are minimal risks in this study as all of these treatments are currently used in the NHS. You will receive one of three routine treatments for OH, however, all medical treatments carry some risk. Although Fludrocortisone is used routinely in the NHS to treat OH, it does not have a specific licence to treat OH; this means that there currently isn't enough information to show whether fludrocortisone works well enough, or is safe enough to be used to treat OH. Midodrine is currently licensed to treat severe OH in standard care.

Whilst we cannot promise that the study will help you directly, the information we get from this study may help to improve the treatment for people with OH.

What happens if I decide I don't want to continue with the treatment I am allocated to?

Treatment arms are randomly allocated; this allows us to achieve three groups of patients that are similar in every respect, with exception of the treatment they receive, and will help us to fairly compare these treatments at the end of the study. To take part, you must be prepared to be allocated to any one of the three treatment options.

You are free to discontinue the study treatment at any time; in this case you would need to discuss this with your doctor in case of the risk of side effects from a sudden withdrawal. If you did stop treatment, it would be valuable for the study if you still continued to complete the questionnaires and attend follow-up visits. Please discuss this with a member of your local study team.

Pregnancy

To take part in the study, women must not be pregnant, breast-feeding or be planning a pregnancy during the time of the study.

When taking fludrocortisone there may be a small risk to the unborn baby of cleft palate (opening or split in the roof of the mouth), poor growth and problems where the glands do not produce enough hormones. Fludrocortisone medication can enter breast milk.

It is not currently known whether midodrine can affect the foetus (unborn baby) or whether it transfers into breast milk. Midodrine has been found to potentially cause development issues in animal foetuses.

To prevent pregnancy during the study, all women of child bearing potential have to use what is called a 'highly effective' method of contraception. Your study team will provide information about what counts as 'highly effective'. If you are allocated to take midodrine or fludrocortisone you will be asked to do a pregnancy test. If you do become pregnant during the course of the study, you must tell your doctor immediately so appropriate action can be discussed.

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

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you decide to withdraw from study activities we could continue to collect routinely collected data from your medical records for study purposes, with your permission, or if you would like to withdraw from study activities and do not want us to collect your routine data after this, we would use your data that was collected up until the point of your withdrawal to include in the study analysis.

Will I receive pay for my participation?

You will not receive payment for taking part in this study.

Will my taking part in the research be kept confidential?

Yes. All of the information collected will be entered on computers that are kept secure and password protected:

- You will be given a unique identification number instead of writing your name on study documents. Staff at your hospital will be able to link this number back to you using your date of birth, name and NHS number.
- Your local study team may contact you to complete study questionnaires if you are unable to attend your study visits.
- Your contact details will never be shared with anyone else outside of the study.
- You will not be named in any results, reports or anything on our website.
- Very occasionally, information might be given during the study that we would have a legal obligation to pass on to others (for instance information which suggested you or others were at risk of harm). In this case, confidentiality would be broken so that we could pass this information to the relevant people. You would be informed of this.

- Site staff will have access to your information during the study to organise study visits as well as for ongoing safety monitoring purposes. At the end of the study, all trial information will be kept in a secure storage area (this is called archiving) for at least 5 years. This makes sure any queries about the running of the study have been answered. All information will be held securely to make sure we protect your confidentiality, after which it will be safely destroyed.

Informing your GP

Your GP will be told that you are taking part in this study. They will be given a copy of this information leaflet. It will also be noted in your hospital medical records so that staff in the hospital know you are taking part in the study

What will happen to the results of the research study?

- The results will be published in medical journals and presented at meetings to other clinicians, researchers and patients.
- A report will be written for the study funder and put on their website.
- All study data that is published will be anonymous. Your identity will always be protected.
- Fully anonymised data may be made available to other researchers to help inform other research studies.
- The results will be available on the study website after the study is completed, or if requested you will be sent a summary of them. Details of the website will be provided to you during the study.

Who is organising and funding this research study?

The central study doctor (also known as the 'Chief Investigator') is Dr James Frith. He is based in Newcastle upon Tyne. The study team also include senior doctors and nurses, university experts in research studies and members of the public.

Study Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust. CONFORM-OH is managed by the Newcastle Clinical Trials Unit on behalf of the Sponsor.

Study funder: the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (reference NIHR127385). This body is funded by the UK government to carry out research for the benefit of the NHS and its patients.

Twenty NHS Hospital Trusts will be taking part in this study. Each trust will have a study doctor, called a Principal Investigator. The Principal Investigator at your NHS Trust is _____

Who has reviewed the study?

The funder reviewed the study plan as part of the application for funding. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given

favourable opinion by the North East- Newcastle & North Tyneside 1 Research Ethics Committee.

How have patients and the public been involved in this research study?

People with OH helped come up with the study question and contributed to its design. They have also contributed to this information leaflet to make sure it is presented in a clear way, and includes important information. People with OH also contribute to the committees who help oversee the running of the study.

Who is providing the study drug?

The study drug is being provided by your hospital or usual pharmacy. It will be prescribed by your hospital doctor or your GP.

What if there is a problem?

If you have a concern about any aspect of this study, you can speak to a member of the study team who will do their best to answer your questions. Further contact details are included at the end of this information leaflet. If you prefer to raise your concerns with someone who is not directly involved in your care, you can confidentially contact <site to localise with local details such as PALS (or other nations equivalent) phone number and/or email address>.

Alternatively, if you wish to make a formal complaint you can contact <site to localise with local details such as site Patient Relations Department (or equivalent) phone number, email address and address>.

Details of the NHS complaints procedure can be obtained from the following website: *http://www.nhs.uk/choiceintheNHS/Rightsandpledges/complaints/Pages/NHScomplaints.aspx*

What if something goes wrong?

We do not expect anything to go wrong as a result of you taking part in this research study. If you have been harmed by taking part in this study, you may have grounds for legal action and could seek compensation through the research sponsors, Newcastle upon Tyne NHS Foundation Trust, who have appropriate insurance-related arrangements in place. If the harm is due to routine clinical treatment or negligence then the NHS indemnity arrangements will apply.

What if I have any questions?

Please ask the doctor who is looking after you, or your local research nurse. They can answer your questions or put you in touch with the Investigator for CONFORM-OH at your hospital. You will find their contact details below.

What happens next?

You can take as long as you need to think about the study and whether you want to take part. Your doctor or, with your permission, a member of the research team will go

through this information leaflet with you and answer any questions before you make your decision.

CONFORM-OH team contact details for your hospital:
For study queries between 09:00-17:00 please contact your local research team:

PI Name Phone
Email

For urgent queries outside of these hours, please call:
XXXXXXXXXXXXXXX and request to speak to XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Supplemental Information regarding the General Data Protection Regulation

The Newcastle upon Tyne Hospitals NHS Foundation Trust (NUTH) is the sponsor for this study based in the United Kingdom and will act as the "data controller" for this study. They are responsible for looking after your information and using it properly.

This study is managed on behalf of the sponsor by the Newcastle Clinical Trials Unit who will act as the "data processor". As data processor, this means that we are responsible for processing personal data on behalf of a controller. We will be using information from you in order to undertake this study, and will keep identifiable information about you for five years.

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 collected. To safeguard your rights, we will use the least amount of personally-identifiable information possible.

You can find out more about how we use your information at: http://www.newcastle-hospitals.org.uk/about-us/freedom-of-information_how-we-use-information.aspx

To find out more about research and general use of patient information please refer to the Health Research Authority Website: https://www.hra.nhs.uk/information-about-patients/

The local study team at your hospital will collect information from you and your medical records for this research study in accordance with our instructions.

The local study team will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the sponsor, Newcastle Clinical Trials Unit and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The local study team will pass these details to Newcastle Clinical Trials Unit along with the information collected from you and/or your medical records. The only people in Newcastle Clinical Trials Unit who will have access to information that identifies you will be people who need to contact you to 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, NHS number or contact details.

The local study team will keep identifiable information about you from this study for five years after the study has finished.

The Newcastle Clinical Trials Unit will collect information about you for this research study from your medical records. NCTU will not provide any identifying information about you to sponsor. We will use this information to monitor the trial.

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.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Thank you for taking the time to read this information leaflet.