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INFORMATION SHEET

Study Title: **AVURT: Aspirin for Venous Ulcers Randomised Trial**

Chief Investigator: **Mr Robert Hinchliffe,**
Reader and Honorary Consultant in Vascular Surgery

Invitation to take part in a study:

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it will involve for you. Please take time to read this information carefully and discuss it with others if you wish. **We will go through the information sheet with you and answer any questions you have.** This should take about 15-20 minutes.

Part 1 of the information sheet tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the study.

Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.

Part 1 – The purpose of the study and what will happen to you if you take part.

What is the purpose of the AVURT study?

Compression (leg bandaging or surgical stockings) therapy is the main treatment for venous leg ulcers. However it can be both uncomfortable and inconvenient for everyday life and ulcers may take many months to heal. There is some evidence that taking daily (300mg) aspirin, in addition to compression therapy might improve the healing of venous leg ulcers. But we are not sure that this is true, so further research is required.

Aspirin is not currently given routinely to patients for leg ulcers, but is commonly used for other conditions and is a cheap drug with relatively few side effects.

In this small study we want to test whether aspirin is better than placebo (dummy medicine) at improving the healing of venous leg ulcers, and if it is safe to use in people with venous leg ulcers. We wish to include 100 patients in the study. If our study shows that taking aspirin could be beneficial we may then decide it is worthwhile carrying out a larger study.

Why have I been invited to take part?

We are inviting patients who have a venous leg ulcer that has been present for more than six weeks, and is larger than 1cm^2, to take part in the study. You will have been invited to take part by a member of your usual medical team or a member of the research team who will also discuss with you what is involved in taking part.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw from the study at any time and without giving a reason. A decision not to take part, or to withdraw at any time, will not affect the standard of care you receive now or in the future.

What will happen to me if I take part?

If you choose to take part in the study and sign a consent form:

- You will have information collected about you to confirm that you are suitable for the study.
- You will have your medical history and any medications you are currently taking recorded. A nurse may also ask you to bring in a copy of your prescriptions if you have any.
- It may be necessary for a nurse or the doctor prescribing your study medication to contact your GP to obtain details to check whether you are suitable for the

study. The study doctor may also need to phone you to check your medical history and ask about medications.

- If you are suitable to take part in the study, you will be given either aspirin or a placebo treatment by chance like the flipping of a coin.
- The study medication can be posted to your home or you can collect it from the clinic depending on what is best for you.
- You will have your leg ulcer photographed in order to measure its size at the beginning, as well as during your normal weekly visits to clinic or during home visits over a period of 25 weeks from when you enter the study. If you have more than one leg ulcer, we shall only take a photo of the largest ulcer. In addition you will have a tracing of your ulcer done at the beginning of the study. If photographs cannot be taken then a tracing of the ulcer will be made instead.
- When you get your aspirin or placebo you will be asked to take it once a day for a maximum of 24 weeks. The study medication should be taken with or after food.
- You will be asked about the following during your routine weekly visits: any change to other medications you are taking, such as if you have stopped or have had a medication dose change; whether you have been able to take the trial medication every day as prescribed; and, any change in your health since the previous visit such as headaches or indigestion. If you are male, you will be asked if your partner has become pregnant.
- Your usual nurse or a research nurse will check the size of your ulcer and its healing during the weekly visits.
- If your ulcer has not healed you will also have it traced during your clinic visit or home visit in week 25.
- If your ulcer has healed, you will receive a follow up phone call from your clinic, in week 25, to check if the ulcer has returned.
- During your first and fifth treatment visits you will be asked about the amount of pain you are having from your venous leg ulcer.

- Your nurse will advise you to stop taking the study medication if your ulcer is confirmed as healed, or if you experience any problems which could be due to the study medication.
- Your participation in the trial will be for 25 weeks unless your ulcer looks like it has healed in week 24 or 25. If this is the case, we would like you to continue in the study for a further two weeks so that we can take weekly photographs of the ulcer, and ask about changes to your medications and to your health since your last visit.
- Your participation in the trial will be for a maximum of 27 weeks.

What do I have to do?

The study will last for 6 months and we want you to:

- Attend your usual leg ulcer clinic regularly /once a week or receive treatment at home as you normally do. If you are unable to attend the clinic or are not seen for a home visit for three consecutive weeks a nurse will phone you to ask about how you have been feeling and about taking the study medication.
- Men and pre-menopausal women will need to use an effective method of birth control (either hormonal in the form of the contraceptive pill or barrier method of birth control accompanied by use of a proprietary spermicidal foam/gel or film; or agree to true abstinence (i.e. withdrawal, calendar, ovulation, and post ovulation are not acceptable methods) from time of consent until 6 weeks after the last dose of the trial medication.
- The study medication can be posted to your home or you can collect it from the clinic depending on what is best for you. If the study medication is posted to your home, we will need you to phone the pharmacy on [redacted] as soon as possible to let them know you have received it.
- Take the study medication (aspirin or placebo) once a day, with or after food, for a maximum of 24 weeks. If your leg ulcer is confirmed as healed before the end of 24 weeks, you will be asked by a member of your medical team to stop taking the medication
- Continue with any other treatment your medical team advises.

- Complete the study questionnaire at the first visit, around 4 weeks later and one at the end of the study. The questionnaire is very short and the research nurse will help you.
- Provide a pain score at your first visit and 5 weeks after you have started in the study (approximately 4 weeks after receiving your study medication).
- Keep a diary of any changes in any other medication throughout the trial and/or bring in prescriptions on a regular basis.
- Provide information about how you have been feeling especially if you have felt unwell.
- You will also be given a 24 hour contact card with the details of St George's Research Pharmacy. If you feel unwell and require urgent treatment you should use your local NHS services and take the card with you so that a health professional can use it if they need to know which treatment you are receiving in the study.
- If your leg ulcer heals during the study, we will give you a card and a stamped addressed envelope for you to notify the research team if the ulcer breaks down again.
- Return your study medication container and any remaining study medication to the clinic at the end of your participation in the study (25 weeks after you entered the study) or earlier if requested by the research team. If the community nurse visits you at your home please ensure the study medication bottle (complete with intact label) is handed over. The bottle will be returned to the Research Pharmacy at St George's Hospital.

What treatment will I get?

Sometimes we don't know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (like flipping a coin). You will get one of two treatments.

Group 1 Aspirin 300mg capsules; **Group 2** Placebo capsules.

One capsule to be taken once every day for a maximum of 24 weeks. The capsule should be taken with or after food. You will be asked to stop taking your study medication before the end of 24 weeks if your leg ulcer is confirmed as healed. Swallow the capsules whole- do not crush or chew. The amount of aspirin is the size of a tablet you might take for a headache.

You will have an equal chance of receiving aspirin or placebo. Neither you, your health care team treating your ulcer or your doctor will know which treatment you are receiving. However, if your doctor needs to find out they can do so.

What are the alternatives for treatment?

The usual option available to you is compression therapy using bandage components or layers wrapped around the leg, or compression hosiery (for example compression stockings). In some cases venous (varicose vein) surgery may be performed. However these options can be uncomfortable, inconvenient for everyday life and take patients many months to heal. In this study we aim to find out if adding daily (300mg) aspirin to compression therapy might improve the healing of venous leg ulcers.

What are the possible benefits of taking part in this study?

If you do take part, you will be contributing to our knowledge about how best to help people with chronic venous leg ulcers. We cannot promise the study will definitely help you as an individual, but we hope that the information and knowledge we get from this study will help improve the treatment of people with venous leg ulcers. If our idea that the addition of aspirin to standard therapy does work, then you could potentially benefit by your ulcer healing faster.

What are the possible disadvantages and risks of taking part?

- You may consider completion of study assessments and taking daily medication as inconvenient.

- There are some medications that should not be taken with aspirin. There are also medications that require caution when taking aspirin. A nurse will ask about any medications you are currently taking before you start participating in the study, as well as frequently (approximately once a week) during study participation. It is important to let your nurse know about the other medications you are taking; and also to let your doctor or pharmacist know that you are taking aspirin when you get new prescriptions or buy other medications from your pharmacy including herbal and complementary medicines.
- Aspirin is not suitable for people with certain conditions, and sometimes a medicine may only be used if extra care is taken. For these reasons, it is important that your doctor and the research team know of any other medical conditions you might have. Your doctors and research team will check carefully that any other medical conditions you might have should not provide cause for concern.
- If you are pregnant or breastfeeding, considering pregnancy or are not taking adequate contraception you will not be able to take part in this study. For women t is also important during the study to let your doctor and the research team know if you get pregnant, or are trying for a baby. If you become pregnant during this study, then you should stop taking the trial medication immediately. If you or your partner becomes pregnant during the course of the study we will then need to ask you questions about your, your partner's health and your unborn child's health until your baby is born.
- Also tell your doctor and the research team if you have ever had an unusual or allergic-type reaction after taking aspirin or a non-steroidal anti-inflammatory drug (NSAID). NSAIDs include ibuprofen, diclofenac, indomethacin and naproxen.
- You must not take any other preparation which contains aspirin, or any non-steroidal anti-inflammatory painkiller without first seeking the advice of a healthcare professional such as a pharmacist or GP.
- You will not be able to participate in this study if you are currently participating in another study evaluating leg ulcer therapies.

What are the possible side effects of Aspirin?

Aspirin is generally safe and most people do not have any problems. But like all medicines, it can cause problems among some people. Aspirin has been used for many years and the problems with aspirin are well known to healthcare professionals. We will check regularly about the known problems.

- The common problems include: feeling sick, indigestion and increased risk of bleeding (for example, an increase in the number of nose bleeds, longer bleeding time or bruising more easily). **If you notice any of these problems tell your doctor or nurse.**
- Other problems include the following: difficulty breathing, stomach irritation, stomach ulcers or bleeding which can be severe (you may develop bloody or black tarry stools, severe stomach pain and vomit blood). Inflammation of the liver causing yellowing of the skin or eyes or tiredness, pain in abdomen, joint or muscles may also occur. **If you experience any of these problems STOP taking this medicine and contact a doctor immediately.**
- Aspirin can also cause allergic reactions which may present as blistered skin, swelling of the face, lips, throat or tongue, difficulty breathing, worsening of asthma, shock. There may also be severe rash involving reddening, peeling and swelling of the skin that resembles severe burns; or severe rash, blisters, or red patches on the skin. **If you experience any of these problems STOP taking this medicine and contact your doctor immediately.**

Speak to your doctor or nurse for advice if you experience any other symptoms which you think may be due to your study medication. In this study aspirin is being given for the healing of venous leg ulcers, and not for pain, cardiovascular or other conditions.

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

Participation in this study should not cost you anything and there will not be any payment for taking part.

Will my taking part in the study be kept confidential?

Yes, we will follow ethical and legal practice. All identifiable information that is collected about you during this study will be kept confidential and secure, disclosed only to

authorised persons such as researchers, the sponsors (St George's University of London representatives),and regulatory authorities (for the monitoring of the quality and safety of the research). Access to your medical records may also be required for this purpose.

Your name or other directly identifiable information will not appear on any materials produced from this study. You will only be known by a unique trial identification number that will be used on all information collected about you for the purposes of the study. The reports of the research findings may also include anonymised venous leg ulcer photographs from participants who have given permission for their photographs to be used in this way.

Your consent form and questionnaires will be stored confidentially and securely at the clinic you attend. Copies of your trial questionnaires and photos will be sent securely to the University of York's Trials Unit that will be processing the emerging study information. The questionnaires and photos will only include your unique trial identification number and will not contain your name.

Study information sent to the University of York will be held there for a minimum period of 12 month after the end of the study. Following this time period the study information may be transferred to St George's University of London for long term storage.

Will my GP be told of my participation in this study?

Yes, if you agree to take part in this study we will tell your GP. We may also contact your GP about your health when this is necessary during the study.

What happens when the study stops?

You will not be provided with any further study medication once your study participation ends. You will however continue to receive your usual treatment in the normal way.

Part 2- More detailed information about the conduct of the study.

What if relevant new information becomes available?

If we get new information about the study medication during the study a research doctor or nurse will tell you and discuss whether you should continue in the study. If you decide not to carry on, your care will be continued outside of the study. If you decide to continue in the study you will be asked to sign an updated consent form.

If your research doctor or nurse considers you should not carry on with the study they will explain the reasons to you. If the study is stopped for any other reason, we will tell you. In both situations your care will be continued outside of the study.

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

Participation in the study is voluntary. You can choose to withdraw from the study at any time.

You may wish to withdraw from the treatment, but continue with the study follow up visits and assessments.

If you choose to also discontinue the follow up visits and assessments, with your permission, we will keep the information that has been collected already but would not collect any more.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer all your questions: contact [Insert names of trial co-ordinators and CI and their contact numbers]

If you wish to complain, or have any concerns about how the study is being carried out, or any other aspects of your care, you may contact:

[INSERT LOCAL INFORMATION, FOR EXAMPLE THE PATIENT ADVICE AND LIAISON SERVICE CONTACT N FORMATION]

The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Sponsor representative at St Georges University of London: [Insert name and contact number]

St Georges, University of London has agreed that if you are harmed as a result of your participation in the study, you will be compensated, provided that, on the balance of probabilities, an injury was caused as a direct result of the intervention or procedures you received during the course of the study. These special compensation arrangements apply where an injury is caused to you that would not have occurred if you were not in the trial. We would not be bound to pay compensation where: The injury resulted from a drug or procedure outside the trial protocol and/or the protocol was not followed. These arrangements do not affect your right to pursue a claim through legal action.

What will happen to the results of the research study?

The results of this study may be published in journals or presented at scientific meetings so other doctors or nurses caring for similar patients can learn from your experience. However, you will not be identified in any reports, publications or presentations. A summary of the results of the study can be sent to you if you like.

Anonymised data that you provide may be used by authorised researchers studying other relevant research projects. Please let us know if you do not agree to this.

Who is organising and funding the research?

St Georges, University of London is the study Sponsor and is taking the overall legal responsibility for the study and will undertake the monitoring and oversight of the participating sites. The study has received funds awarded by the NHS National Institute for Health Research, Health Technology Assessment Programme [grant number NIHR HTA: 13/87/08]

The research team is led by Mr Robert Hinchliffe, Reader in Vascular Sciences and Honorary Consultant in Vascular Surgery, St George's Vascular Institute, St George's

University of London and St George's Healthcare NHS Trust. The trial is managed by the York Trials Unit at the University of York.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and approved by **[Insert name here]** Research Ethics Committee. It has also been reviewed by your local hospital Trust Research and Development Department.

Further Information and Contact Details

If you require further information about this study you can contact the following:

Trial Co-ordinators: [Insert names and contact numbers]

Sponsor Representative: [Insert name and contact number]

If you are unhappy with any aspect of this study, or have any concerns please contact:

Trial Co-ordinators: [Insert names and contact numbers]**, or**

Chief Investigator: [Insert name and contact number]

Call the following number Monday – Friday 09:00hrs – 17:25hrs to let the pharmacy know you have received your AVURT study medication: [Insert contact number]

Other useful contact numbers

Your Research Nurse or Nurse

Name: **[Insert site contact details]**

Tel. Number: **[Insert site contact details]**