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Participant Information Sheet

UCON Trial: Ulipristal versus Coil for the Management of Heavy Menstrual Bleeding

Local Lead Doctor	[NAME HERE] + TELEPHONE NUMBER + EMAIL ADDRESS
Research Nurse	[NAME HERE] + TELEPHONE NUMBER + EMAIL ADDRESS

Invitation to take part in this research study

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand this why this research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information.

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

Part 2 gives you more detailed information about the conduct of the trial.

Part 1

What treatments are available for heavy menstrual bleeding?

Previous research has shown that a hormone releasing coil, which is fitted inside the womb, is effective in reducing the impact and symptoms of heavy menstrual bleeding. Other medical treatments, including the contraceptive pill and non-hormonal treatments also reduce bleeding, but not as well as the coil. A few years ago, a drug called ulipristal has been found to quickly reduce bleeding in women with large, non-cancerous growths in the womb, known as fibroids. It is not known whether this drug is effective in reducing the impact of heavy menstrual bleeding in women who do not have fibroids, or have small, insignificant fibroids. It is also unclear how ulipristal stops menstrual bleeding and its effect on the womb lining.

What is the purpose of the study?

Both ulipristal tablets and the hormone releasing coil are safe, effective treatments, each with advantages and disadvantages, but doctors do not know which women will benefit from either treatment. Since the way the treatments work and are used are different, it is important to compare them against each other.

Why have I been asked to take part?

All women visiting their doctor because they feel that they need treatment for heavy periods are being invited by hospitals to take part in UCON. We are aiming to recruit 220 women with heavy menstrual bleeding to take part.

If you are currently trying to get pregnant, or think that you might want to get pregnant in the next year, then the UCON trial is not suitable for you, as one of the treatments is a contraceptive.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the trial will not affect the healthcare that you receive, or your legal rights.

Will I need to undergo any tests before I can participate?

At the first clinic visit, if you are willing to take part in the UCON trial you will be asked to sign a consent form. Your Consultant Gynaecologist will ask about your symptoms and any treatments you have tried. You will have an ultrasound scan and a sample of tissue taken from your womb (called a biopsy). This is to confirm that there are no obvious reasons for your bleeding, such as large fibroids, and that the womb lining is normal.

We need to be certain that you don't have any undiagnosed liver problems, so you will be asked to have a blood test. This will be taken at the same time as the biopsy and will be less than a teaspoon of blood from the arm.

We will also give you a diary chart to record some details about your next period.

What will happen next if I can take part?

At your second clinic appointment you will be seen by a clinician, who will review your biopsy and blood test results with you. If an obvious cause for your bleeding is found, your doctor will discuss treatment options with you, but you will not be eligible to take part in the UCON study.

If you are eligible for the UCON Trial, the research nurse will collect your completed diary and give you a questionnaire booklet to complete. The questionnaires ask about your bleeding and the impact of your symptoms on your life. If you are sexually active, you will need to take a pregnancy test.

If I take part, will I have the coil or the ulipristal tablets?

Neither you nor your doctor can choose which treatment you receive. The decision is made randomly by computer at the UCON trial office. This is essential so that a fair comparison can be made between the two treatment groups. Dividing people into groups in this way is called a 'randomised clinical trial' and it is the standard and most reliable way of comparing different treatments. There is an equal chance of being allocated to the ulipristal group or the coil group (please see Figure 1 for a summary of the patient pathway).

If I am allocated to the ulipristal group, how will I take them?

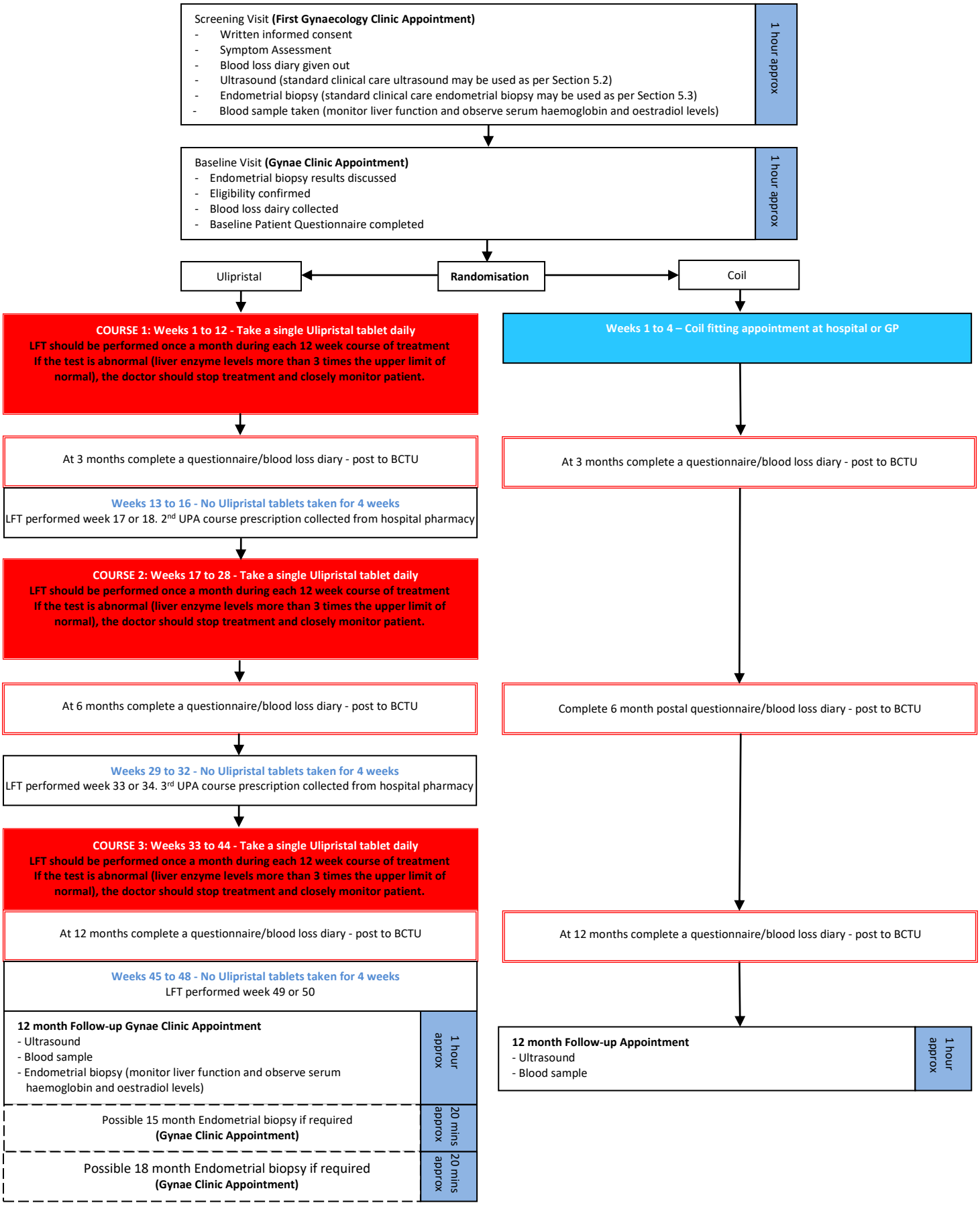
You will be given a free prescription of 36 weeks of tablets. You must take one tablet every day for 12 continuous weeks and then stop treatment for 4 weeks. During this time off treatment, you may have light bleeding. You will repeat this course of 12 weeks treatment and 4 weeks off treatment twice more. Your periods should return to being regular after that, but we do not know if they will be as heavy as before you started the treatment.

Once you complete your current course of ulipristal, your periods should return but we do not know if they will be as heavy as before you started the treatment.

If you are taking ulipristal and are sexually active, you will have to use barrier methods of contraception (such as condoms or the cap), as ulipristal is not a contraceptive.

You will also need to provide the research team with a monthly blood sample to check your liver function.
This will continue for the duration of each 12 week course of tablets, with a final blood sample 2 - 4 weeks after you have taken your last ulipristal tablet. Each blood sample will require approximately 5ml (1 teaspoon) of blood to be taken, and there will be 13 blood samples in total.

Figure 1: Patient pathway



If I am allocated to the coil group, how will this be given?

The coil will be fitted by a hospital doctor/GP inside your womb and once in, you will not be able to feel that it is there. The coil usually takes around 10 minutes to fit and some women may experience period-like pain during the procedure, but this normally settles within a few minutes to a few hours. To reduce the risk of pain, your doctor may give you a painkiller beforehand, or afterwards, or use a pain-relieving cream. If the pain did become unacceptable your doctor would immediately stop the procedure.

Most women have spotting (a small amount of blood loss) or an irregularity of their bleeding pattern for the first 3-6 months after the coil is fitted before a reduction in blood loss is achieved. Overall, there are likely to be fewer days bleeding in each month and eventually, some women's periods may even stop completely.

The coil is also a contraceptive device and therefore you are very unlikely to become pregnant while you have the coil in place. So, if you think that you may wish to try for a baby in the next year, you should not take part in this study. You can have the coil removed at any time and you may soon be able to get pregnant. Those wishing to continue with the coil must have it replaced every five years.

How will my progress be followed?

You will be asked to complete the diary chart and the questionnaire booklet again at about 3, 6 and 12 months. Women in the coil group will also be asked to provide another small blood sample at 12 months. For women in the ulipristal group, it is important that you have another biopsy 4 weeks after you stop treatment, as well as the final blood sample. If you complete the 3 courses of tablets, this will be at about 12 months after the start of treatment.

What are the possible benefits of taking part?

You may or may not get a direct benefit from taking part in this study.

It is hoped that the findings from the trial demonstrate ulipristal as a safe, acceptable and more effective treatment of heavy menstrual bleeding.

What are the possible disadvantages and risks of taking part?

The lining of the womb consists of a layer of cells that grow and shed during the menstrual cycle. Ulipristal may cause non-cancerous changes in the womb lining of some women. If the biopsy taken 4 weeks after stopping treatment shows any changes, you will be invited back for further biopsies, but nearly all changes are reversed within 6 months of stopping treatment. The reasons why ulipristal causes these changes is unclear and we hope the UCON study will help doctors understand why they happen.

Most women find the coil helpful with their heavy bleeding, but some also find their periods become irregular. About one in three women ask for the coil to be removed within two years.

Women may experience a wide range of symptoms during their menstrual cycle with and without treatment.

These symptoms can include abdominal and back pain, nausea, acne, emotional changes, swelling and breast tenderness. In addition to these symptoms, a minority of women may also experience headaches, vaginal discharge, hot flushes, sweating, hair growth and ovarian cysts whilst receiving these treatments. These symptoms are usually experienced infrequently and are short-lived in nature.

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 decisions.

Ulipristal was under investigation by the European Medicines Agency from December 2017 and was temporarily suspended and not allowed to be prescribed. Eight reports of serious liver injury were reported in Europe in an estimated 740,000 women using ulipristal for uterine fibroids. It is still unclear whether the use of ulipristal led to these liver problems or there were underlying reasons. However, in order to safeguard patients, recommendations have been issued that women who are take ulipristal should have blood tests taken at least once a month to check their liver function. A final liver test is also needed 2-4 weeks after stopping treatment. The UK Medicines and Healthcare Products Regulatory Authority allowed use of ulipristal to resume in August 2018.

Please contact the research team immediately if you experience any of the following symptoms:

- nausea (feeling sick)
- vomiting
- upper belly pain
- lack of appetite
- tiredness
- yellowing of the eyes or skin

Part 2

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

If you do decide to take part, you are entitled to withdraw from the study at any time, without having to give a reason, and this will not affect the standard of your medical care in any way. We would like to use the data collected about you up to your withdrawal. Even if you no longer wish to complete the questionnaires, we would like to continue to collect a few important details from your GP, such as other treatments, if you get pregnant or when your baby is born. In the unlikely event of you losing the ability to give continued consent during the study we would like to keep data that we have already collected about you for research purposes.

What if there is a problem?

If you have a concern about any aspect of this study please contact the Local Lead Doctor for UCON stated on page 1 of this document who will do their best to answer your questions. If you would like to discuss this study with someone independent of the study your local Patient Advice and Liaison Services (PALS) group or local equivalent group at the hospital can help.

If you wish to make a complaint about the study please contact:

[Insert Trust complaints team details here]

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against your local NHS Organisation. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in the study be kept confidential?

Yes, if you decide to take part in the UCON trial, all information which is collected about you during the course of the research will be kept strictly confidential in the same way as your medical records.

Information about your condition and progress will be sent by your hospital to the UCON trial office at the University of Birmingham Clinical Trials Unit. This information will be put into a computer and analysed by the UCON Trial Office team. The questionnaires will not contain your name and will be identified using a code number. The biopsy samples will be assessed first at your local hospital and sent for a second expert review at Edinburgh (NHS Lothian) but they too will only be identified by a code number.

All information will be held securely and in strict confidence. No named information about you will be published in the study report. Information held by the NHS may be used to keep in touch with participants and follow up their health status. Occasionally, inspections of clinical study data are undertaken to ensure that, for example, all participants have given consent to take part, so a copy of the consent form will be sent to the UCON Trial

Office. Responsible members of the University of Edinburgh or University of Birmingham, or the NHS organisation may also be given access to data to ensure we are complying with regulations. But, apart from this, only the study organisers will have access to the data.

If you demonstrate any signs or symptoms of liver damage (including results from your liver function blood tests) the research team may refer you to a liver specialist for further care.

If you are allocated ulipristal, your gynaecologist must contact your GP to notify them of the safety information for ulipristal and inform them of the additional tests liver function tests. If you are allocated the coil, with your consent, your gynaecologist will informed your GP that you are taking part.

What happens when the study is finished?

In line with the Medicines for Human Use (Clinical Trials) Regulations, and General Data Protection Regulation (GDPR) 2018 once data collection is complete on all participants, at the end of the study, all data will be stored for at least 25 years. Arrangements for confidential destruction will then be made at the appropriate time.

The endometrial biopsy samples will be returned to the original hospitals.

What will happen to the results of the study?

At the end of the trial, about two years after the last participant was recruited, the results will be published in a scientific journal. Your hospital doctor can provide you with a copy of this publication if you are interested. We will also publicise the results on the trial's website www.birmingham.ac.uk/ucon. Only anonymous data will be published and your name will not appear in any report, presentation or publication.

Who is funding and organising the research?

The UCON trial is being co-ordinated by the University of Birmingham Clinical Trials Unit. The trial is funded by the National Institute for Health Research through the Efficacy and Mechanism Evaluation programme (NIHR EME). Your doctor will not be paid for including you in this trial.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, wellbeing and dignity.

This trial has been reviewed and given favourable ethical opinion by **NRES Committee London - Bloomsbury (Ref: 14/LO/1602)**. Research Ethics Committees include healthcare professionals as well as non-medical people, and are completely independent from anyone organising the trial. Further details about the National Research Ethics Service can be found at *http://www.hra.nhs.uk/about-the-hra/*. This trial has also been reviewed and approved by the Medicines and Healthcare products Regulatory Agency (MHRA) and NHS management.

Do you have any further questions?

Having read this leaflet, it is hoped that you will choose to take part in the UCON trial. If you have any questions about the study now or later feel free to ask your gynaecologist or clinic nurse. Their names and telephone

numbers are given on the front of this leaflet. Please take the time before your next appointment to decide whether you wish to take part in the UCON trial. You may like to discuss your decision with friends or relatives.

The UK Clinical Research Collaboration has produced a guide entitled, 'Understanding Clinical Trials'. This can be down loaded from their website: www.ukcrn.org.uk and maybe useful if you require general information about research. If you require specific information about the research project please contact any of the hospital UCON staff listed on the front page. The UCON Local Lead Investigator can give you more advice about the treatment options.

Information regarding heavy menstrual bleeding is available from Women's Health Concern,
T – 0845 123 2319, www.womens-health-concern.org.

Alternatively, you may visit the Birmingham Clinical Trials Unit study website at www.birmingham.ac.uk/ucon or contact the Birmingham Clinical Trials Unit using the details below.

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Please note that the UCON trial office does not offer advice on clinical queries.
Thank you for taking the time to read this information sheet.