Participant Information Sheet (PIS)

Trial of Ondansetron as a Parkinson's HAllucinations Treatment. The TOP HAT Trial.

1. Invitation to participate in a research study

We would like to invite you to take part in our research study. Before you decide it is important for you to understand why the research is being done and what it will involve. One of our team will go through the information sheet with you over the telephone and answer any questions you might have. Please read the following information carefully and discuss it with relatives, friends or doctor if you wish. Please ask us if there is anything that is not clear or if you would like more information.

Please take time to decide whether or not you wish to take part.

2. Why have I been chosen?

You are being asked to participate in this research study of ondansetron because you have Parkinson's disease or Lewy Body Dementia and are experiencing visual hallucinations – seeing things that are not there. You have been given this information sheet because you or the person who cares for you, have expressed an interest in the study.

The study will recruit 306 people over the age of 18 years with Parkinson's disease or Lewy Body Dementia who are experiencing visual hallucinations at least weekly, which are not due to an underlying infection, and have not responded to altering or reducing Parkinson's or Lewy Body Dementia medication. Recruitment will take place over 2 years in 20-25 NHS clinics.

3. What is the Purpose of the Study?

The study aims to determine whether ondansetron, a drug already used in the NHS as an anti-sickness treatment, will be both effective and well tolerated as a treatment for visual hallucinations in people with Parkinson's or Lewy Body Dementia.

TOP HAT is what is called a clinical trial, in which ondansetron will be compared to placebo, a tablet that looks identical but contains no drug. Treatment will last for 12 weeks, with telephone follow up for a further 12 weeks once treatment ends.

Ondansetron was identified as a promising treatment for visual hallucinations in the early 1990s, in two small studies (7 people, and 16 people) in people with Parkinson's who were hospitalized because they had persistent severe hallucinations.

The drug was effective in reducing visual hallucinations in all but one person, with only mild side effects of constipation and headache and no worsening of Parkinson's symptoms. Further studies were not carried out at the time because the drug was extremely expensive. Costs are now similar to standard treatment and a larger study is timely and necessary.

4. Why is the study important?

Drug treatment options for visual hallucinations in people with Parkinson's disease and Lewy Body Dementia are limited to medications that were developed to treat symptoms in people with schizophrenia. These drugs, described as antipsychotics, can cause significant side effects including sleepiness, falls, and a worsening of Parkinson's disease and Lewy Body Dementia symptoms, such as tremor. The most effective of these, clozapine, can only be given in specialist clinics as weekly blood tests are needed to monitor safety. It is really important that we identify and test alternative treatments in clinical trials led by NHS clinicians. If ondansetron proves to be effective and safe as a treatment for visual hallucinations in people with Parkinson's disease or Lewy Body Dementia the fact that it is already used in the NHS to treat sickness, and is of low cost, will speed its progression to use in NHS clinics.

5. What measures have been taken to reduce risk of exposure to coronavirus (COVID-19)?

The trial assessments and procedures have been reviewed and changes made to minimise personal contact, to reduce the risk of exposure to coronavirus in hospitals or clinics.

Three brief face-to-face assessments will be necessary, as they involve taking a blood sample, an electrocardiogram (ECG) or blood pressure check, to ensure it is safe for you to take part and to monitor health and safety while taking the study drug.

As an alternative to a 12-lead ECG, we will be using a small, hand held mobile device. You will simply be able to place two fingers on each side (right and left) of the upper surface of the app, and then rest the lower surface of the app on the left knee or ankle for 20-30 seconds.

The device is linked to the clinician's smart phone and, once the clinician receives the information, they will enter your study identification number before sending it via a secure link to the trial email account. The device is shown below:

All other assessments will be completed over the telephone and we also aim to use video consultation for assessments that require longer conversations.

During the first face to face assessment, the research team will check that you are able to access the video link from a desk top computer, a smart phone, tablet or iPad. If this is not possible, the assessment will be done by telephone.

If you are able to use the video link, we will collect information on how satisfied you are with the video consultation.

6. What happens if I suspect or am confirmed to have COVID-19?

If you think that you may have COVD-19 symptoms whilst taking part in the trial, you will be asked to self isolate until a test has been carried out. If the test is positive, it may be necessary to delay any planned face to face assessments or may involve a visit to your home by one of the study team, who will wear Personal Protective Equipment (PPE).

All use of PPE, and other testing (or tracing) procedures will follow the scientific advice, National guidance and the local policies in the NHS Trust and clinic overseeing your care.

7. Recent review of safety

As in all clinical trials, an independent team - called the Data Safety and Monitoring Board (DSMB) - was set up to monitor known side effects of ondansetron (such as heart rate and rhythm, constipation, headache) and other events such as falls, attendance at A&E, hospital admissions and deaths. After the first 100 participants had taken part in the study a preliminary analysis was carried out to look at how well the study drug was tolerated and address any safety concerns as promptly as possible.

After looking at this data in February 2024, there appeared to be more safety issues in the ondansetron than placebo arm and the DSMB recommended that recruitment should pause while the data underwent review. This was purely a precautionary measure while a more detailed review of safety data happened.

All of the data has since been checked and two reporting errors identified in the first 100 participants. This has been corrected and data from an additional 68 participants has also been reviewed. Based on this updated information, the DSMB informed us there was no evidence of excess safety concerns in the treatment arm and advised that recruitment restart.

8. Do I have to take part?

No, it is up to you to decide whether or not to take part. Take your time, discuss things with your spouse/partner/carer/relative/doctor and ask us about anything that is not clear or if you would like more information. If you decide not to take part your treatment will not be affected

by your decision. You are free to withdraw at any time without explanation and your subsequent treatment will not be affected.

If you do decide to take part you will be given a copy of this information sheet to keep. You will be asked to sign a consent form. You will be given a copy of your signed consent form and we will inform your GP about your involvement in the project.

If you decide to take part you are still free to withdraw at any time, without giving a reason, and this will not affect your subsequent treatment.

9. What will happen to me if I wish to take part?

One of the research team will arrange a time to talk with you (and a spouse, partner, family member or other if you wish) on the phone to discuss the study in more detail and answer any questions you may have. This should take around 45 minutes.

The research team will be part of your local clinic/NHS trust and they will be in close contact with the doctor and/or team who are responsible for your clinical care. As they are part of your local care team, they may also need to access your medical notes.

Every effort will be made to provide time and support to enable you to make your own decision whether or not to participate in the study. This includes providing information in a way that is accessible to you. If you wish you may involve a family member, friend or other advocate to help you to make the decision.

You will be asked to provide verbal and written consent over the telephone initially, to avoid a clinic visit. The form will be checked and countersigned when the researcher sees you face-to-face at the screening visit.

If you do not feel able to give consent by yourself, a relative/carer/close friend or health professional not involved with the study will be asked to act as a legal representative and provide or withdraw consent to continue with the study on your behalf. Even if he/she consents on your behalf if you tell the study doctor that you do not wish to participate this will always be respected.

10. Before starting treatment

If you agree to take part in the study, a member from your local research team will call you on the telephone to ask some brief questions about the hallucinations, to find out how often they are happening and how they affect you in your daily life. A member of the local research team will also review and discuss your medical history and current state of health with you (and with your GP if you agree) to make sure there is nothing to prevent you from taking part in the study. A brief test of your memory will also be made.

If you have another severe health condition, such as liver disease, or a very slow heart rate, you may not be able to take part.

If you are taking a medication called apomorphine you will not be able to take part, unless you and your doctor decide that it is safe to switch to an alternative Parkinson's disease or Lewy Body Dementia treatment.

If you are currently prescribed ondansetron (or similar drugs granisetron, tropisetron) as an anti-sickness medication, or have had an allergic reaction to any of these anti-sickness medications, it will not be safe for you to take part.

If you are prescribed medication that may increase the risk of any potential side effects, he/she will be advised not to increase the dose of medication while taking the study drug. Your GP will also be asked not to increase the dose of medication during the 12 week treatment period. If an increase in the medication is required, GPs will be asked to contact the local team to find out if any extra monitoring is needed.

If you are pregnant, you will not be able to take part, as ondansetron can increase the risk of a baby being born with a cleft lip or cleft palate.

If you or your partner are of child-bearing potential you will be asked to use effective contraception during the study and for 6 weeks after the last dose of the study drug.

If you are a woman of child-bearing potential, you will be asked to have further pregnancy testing after 6 and 12 weeks treatment and 6 weeks after the study drug has been discontinued.

The research team will then arrange a brief face-to-face screening visit, which may take place either at a clinic or your home. The visit should take no longer than 20 minutes and the following checks will be made:

- An electrocardiogram (ECG), which will be taken using a hand held, mobile
- A routine blood sample which includes liver function tests
- Blood pressure and pulse check
- Height and weight
- Brief test of language and motor skills
- a urine pregnancy test if you are a woman of child-bearing potential
- Parkinson's disease and Lewy Body Dementia symptoms will be assessed by observation, in line with social distancing guidelines, and will not require any physical contact.

During this screening visit, a member of the team will also check that you are able to access the link to the video consultation via a desk top PC, laptop, smart phone or tablet.

A member of the team will be able to answer any questions about how this will work to make sure you are happy about accessing the service. If this is not possible, the assessments will happen via the telephone.

11. What will happen next?

Taking part will involve being allocated (randomly via a computerized system) to receive drug or placebo for 12 weeks, and there will be further follow up for 12 weeks once treatment ends. The research team will carry out randomisation by accessing a secure, web-based system. Neither the prescribing clinicians nor participants will know which treatment you are taking.

The study drug will be delivered to your home by a courier. In order to arrange this, we will need your consent to share your address with the trial medication distributors, Modepharma and the courier. This information will not be used for any other purpose and will be destroyed at the end of the trial. Your study number will be used instead of your name on the delivery package, so it is important that you know what it is. Your researcher will remind you of this before the medication arrives. Please do not start the study drug and wait until the one of team instructs you to start at the baseline assessment.

It is important for you to know that the usual treatment for hallucinations, a drug called quetiapine, will be made available to you at any point during the study if your symptoms require further treatment. One of the things we will be comparing is the proportion of people in each treatment arm who need quetiapine in addition to the study drug. If your symptoms

are still not improving, the study doctor will discuss the possibility of withdrawing you from the study medication and discuss other treatment options that might be available to you. Whether or not you remain on the study drug we will continue to follow your progress to the end of the study, to obtain an accurate comparison of the drug and placebo treated groups.

The assessments have been summarised in the following paragraphs and in a table:

- Baseline assessment:

Before you start taking the study drug, one of the team will arrange a video consultation with you to first of all check that two packs of the study drug have arrived. They will confirm the pack numbers with you and will inform you which pack you need to start taking first as well as how and when to take the medication. They will also take you through several questionnaires, which will help us to understand more about the hallucinations, and any accompanying symptoms, such as delusions (false beliefs that may be linked to the hallucinations). You will also be asked about Parkinson's disease or Lewy Body Dementia symptoms (tremor, anxiety, sleep disturbance), memory, and quality of life. If you are female and of child bearing potential you will also have a urine pregnancy test. You will be asked some brief questions about your recent use of health care services such as recent visits to your GP and community services. Finally, you will be asked about your experience of participating in the video consultation.

- Finding the best dose of the study drug for you:

You will be asked to open one pack of medication and to take one tablet for the first 2 weeks. You will be asked to put the second pack of medication away as you will not need it until week 6. You will then receive a telephone call from one of the team, to see how you are getting on. If there are no side effects, the dose will increase to 2 tablets daily (morning and evening) for a further 2 weeks. At the end of week 4 you will receive another telephone call and, if you are tolerating the drug well, there will be a further increase to 3 tablets daily (1 each morning, 2 each evening).

The decision to increase the dose will be guided by any side effects you report, the impact they are having on your life, and how likely they are to be related to the study drug. Please tell the person who calls you if there has been any change in your health, even it if is minor. During each of the telephone calls, you will also be asked about any changes to your prescribed medication.

- Assessments after 6 and 12 weeks treatment:

At the end of 6 weeks, a member of the team will arrange a video consultation at a time that is convenient to you. You will be asked similar questions to those asked at baseline, plus extra questions relating to any side effects or changes in prescribed medication. You will also be asked to comment on your experience of the video consultation.

After this, a member of the team will arrange a brief face-to-face visit (at your home or clinic).

If the assessment is happening in a clinic, please bring your medication with you.

The ECG will be repeated to ensure that the study drug has not affected your heart rate or rhythm, and a blood sample (equivalent to a teaspoon of blood) will be taken, to measure blood drug concentrations. If you are a woman with child-bearing potential, pregnancy testing will be carried out. Your Parkinson's disease or Lewy Body Dementia symptoms will also be assessed, but it will not require contact.

A member of the team will collect any remaining medication from the first pack and will take them away to arrange disposal.

You will then continue treatment with the study drug from the second pack, for a further 6 weeks, at the dose recommended by the research team.

The week 12 assessment will be very similar to the one at 6 weeks, with a brief face visit to obtain a blood sample. This time the amount of blood will be equivalent to three teaspoons; one teaspoon will be used to measure blood drug concentrations, and the other two will be sent to the local laboratory to check your liver function.

If you are coming to clinic for the face-to-face assessments, please bring any unused tablets from the second pack with you as the researcher will need to collect them from you for disposal. A pregnancy test will be carried out if you are a woman with child-bearing potential.

You will be given a urinary pregnancy testing kit to take away with you. You will be advised to continue to use effective contraceptive for a further 6 weeks, and asked to carry out a further pregnancy test at the end of the 6 weeks.

You will be asked some brief questions about your recent use of health care services such as recent visits to your GP and community services over the past 12 weeks. At the end of the

face to face visit, the clinician will check that you have access to the video link, and the remainder of the questions will be carried out via a video consultation.

- Telephone follow up once treatment ends:

Further follow up will happen via the telephone, 6 and 12 weeks after you have stopped taking the study drug. During the telephone calls you will be asked some questions about your hallucinations and related symptoms, quality of life and any changes in your health or prescribed medication.

If you are a woman with child-bearing potential you will be asked the result of the pregnancy test.

During the 12 week telephone call (12 weeks after stopping the study drug), you will be asked some brief questions about your recent use of health care services such as recent visits to your GP and community services over the past 12 weeks.

Summary of what will happen if you take part in the TOP HAT Trial	
Assessment timing and length	What will happen during the assessment. Please note, the video consultations and telephone assessments were put in place to reduce face to face contact during COVID, but there is flexibility, depending on what is feasible and preferable for you and the research team.
Baseline - video consultation before starting the study drug 30 minutes	This assessment will take place via a video consultation and will involve: ✓ Check that study drug arrived ✓ Study questionnaires ✓ Evaluation of video consultation experience ✓ Brief questions about recent use of health care services ✓ Instructions on starting the study medication and on how much to take daily.
Telephone call to monitor safety,	The dose of the study drug will increase in weeks 3 and 5, unless there are side effects:

2 and 4 weeks 15 minutes	✓ Study questionnaire (brief) ✓ Side effect checklist ✓ Medication changes A decision will be made as to whether you should increase the dose of the study drug, stay the same, or decrease
6 week video consultation 30 minutes 6 week face to face assessment 20 minutes	This assessment will take place via video consultation and will involve: ✓ Study questionnaires ✓ Side effect checklist ✓ Medication changes * * * A brief face to face assessment will then be arranged by the research team and may take place in your home or in clinic, depending on your local team arrangements and your needs. This will involve: ✓ Blood test to measure concentrations of the study drug ✓ Evaluate video conference experience ✓ Follow up ECG ✓ Severity of motor symptoms check ✓ Urinary pregnancy test (women with child-bearing potential) Any unused medication from the first pack will be counted and collected for disposal.
12 week face to face assessment 20 minutes	See above, similar to 6 week assessment. You will be asked to bring any unused medication to the clinic (unless you have arranged for a home visit) ✓ Blood test to measure concentrations of the study drug and to check your liver function ✓ Severity of motor symptoms check ✓ Quick language and motor skills test

	✓ Urinary pregnancy test (women with child-bearing potential) * * * Video consultation (see above, similar to 6 week assessment). ✓ Study questionnaires ✓ Side effect checklist ✓ Medication changes ✓ Brief test of memory ✓ Brief questions about recent use of health care services ✓ Evaluation of video consultation End of treatment with the study drug
Telephone follow up, 18 and 24 weeks 15 minutes	The team will keep in touch via the telephone once treatment ends, to see how you are getting on: ✓ Study questionnaires (brief) ✓ Medication changes ✓ You will be asked the result of the urinary pregnancy test (18 weeks) ✓ Brief questions about recent use of health care services (24 weeks)

12. Expenses and payments

Travel expenses are available to cover your trips to and from the face-to-face assessments (if these are not conducted at your home), and for any unscheduled assessments that may be necessary. You will be able to complete an expense claim form with your details including name, address, bank details. Your local researchers will then be able to send this form to the central team for processing to arrange for your expense claims to be approved and payment arranged.

13. What will I have to do?

- Take the study drug as directed:

The study team will give clear instructions about how many tablets you will need to take and will check each time they call you or via video consultation.

- Complete study assessments:

We have kept face-to-face assessment to a minimum and there will be only three brief face-to-face sessions which will be at screening, week 6 and week 12. These assessments may happen in your local clinic, or a trial facility /research clinic, or at your home. This will depend on the local arrangements and on your needs. If you are travelling to clinic, please bring the blister pack with the study medication with you. All other assessments will be completed via video consultation and further follow-up will be conducted on the telephone.

- Taking other medication:

Your involvement in the study will not interfere with other Parkinson's disease or Lewy Body Dementia treatments you are currently taking or may be prescribed during the course of the study.

If any of your regular medications may increase the risk of potential side effects, you will have been asked not to increase the dose(s) while taking the study drug. Your GP will also have been informed and, if he/she feels it is necessary for this medication to increase, the study team will be contacted to find out if any additional telephone or other follow up is needed

- Can I take part in other research?

While participating in this research study, you should **not** take part in any other research study. This is to protect you from possible injury arising from such things as extra blood samples, possible unwanted reactions between research drugs, or other problems.

14. What are the alternatives for treatment?

Current treatment options for visual hallucinations in people with Parkinson's disease or Lewy Body Dementia are limited to antipsychotic medications that were developed to treat

symptoms in people with schizophrenia. These drugs, can cause significant side effects including sleepiness, falls, and a worsening of Parkinson's disease or Lewy Body Dementia symptoms, such as tremor. The most effective of these, clozapine, can only be given in specialist clinics as weekly blood tests are needed to monitor safety.

Quetiapine, which we have already mentioned, is the safest of these and is the usual treatment prescribed in NHS clinics and will be made available to you if you need additional treatment for your symptoms at any point in the study.

15. What are the possible disadvantages and risks of taking part?

- Assessments:

Taking part in the study will involve a number of assessments and some investment of time. We have kept the number of face-to-face assessments and other procedures including blood tests and ECG to a minimum, but you may nevertheless experience some fatigue or discomfort from participating in these activities

- Will my symptoms be treated?

There is a risk that taking part in the study will leave your symptoms untreated, as you have a 50% chance of receiving placebo. To reduce this risk, quetiapine will be made available if you and your doctor feel that you need additional medication to help with your symptoms.

- Is ondansetron safe?

Ondansetron is licensed for short term use as an anti-sickness treatment and has had extensive safety testing. The long term safety of ondansetron has not been examined, as people usually take the drug for a short time, but there are no anticipated effects of taking the drug for 12 weeks.

We know from previous studies that the optimum dose – the one that is effective without causing side effects – varies between people. To account for these differences, we will be increasing the dose of the study drug gradually over the first 6 weeks, to ensure that you are on the dose that is right for you.

- Pregnancy related risks and guidance:

Research studies that have examined information on ondansetron use in pregnant women suggests that ondansetron may slightly increase the risk of a baby being born with a cleft lip or cleft palate when administered during the first trimester of pregnancy.

In the general population, the risk of a baby being born with a cleft lip with or without a cleft palate is estimated as 10 babies per 10 000 births.

A study that examined data from 1.8 million pregnancies showed that, compared to the risk in the general population, use of ondansetron in the first trimester increased the risk of oral clefts. The extent of the risk was 3 additional cases per 10 000 women treated (13 babies per 10 000 births).

Animal studies have not shown any harmful effects in relation to pregnancy.

Guidance from the UK regulatory body for medicines suggests that ondansetron should not be used during the first trimester of pregnancy.

Tests have also shown that ondansetron passes into the milk of babies during breast feeding and it is recommended that mothers receiving ondansetron should not breast-feed their babies.

For this reason, premenopausal female participants will be asked to have a negative urine pregnancy test within 7 days prior to taking part and will be asked to use effective contraception from the time consent is signed until 6 weeks after treatment with the study drug ends. Effective contraception refers to hormonal or barrier method of birth control, or true abstinence.

Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence, withdrawal, spermicides only or lactational amenorrhoea method for the duration of a trial, are not acceptable methods of contraception.

The same applies to premenopausal female partners of men who are participating in the study. Women are considered not of child bearing potential if they are surgically sterile (i.e. they have undergone a hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or they are postmenopausal.

Male participants with partners of childbearing potential are responsible for informing their partner of the possible risks to an unborn child of the medicine they will be taking in this study.

For women: If you become pregnant during your time on this study, you must tell your doctor. Your doctor will withdraw you from the study and will find out whether you have been allocated to the ondansetron treatment arm. If this is the case, your doctor will ensure that your obstetrician will be informed that you have taken part in this study. With your consent, we will request from your obstetrician to send us information on the pregnancy and child's birth that is relevant to your participation on the study. If this relevant information needs to be reported to the sponsor, ethics committee or UK regulatory body for medicines, the information will be anonymised so that neither the new born child nor you can be identified.

For men: If your partner becomes pregnant during your time on this study, please tell your doctor, so that he/she can give your partner information on why we may wish to follow up her pregnancy and seek her specific consent to access her medical notes.

16. What are the side effects of any treatment received when taking part?

- Common side effects:

The most commonly reported side effects of ondansetron are headache (more than 10% of people), constipation and flushing (both of which have been reported in less than 10% of people). We know that constipation is more common in people with Parkinson's disease and Lewy Body Dementia and we will be asking you about any medications you are currently taking for this (for example macrogol, brand names Movicol, Laxido, CosmoCol, Molaxole or Molative), before you start treatment. If you experience worsening of constipation, please increase the amount of macrogol or other prescribed medication. If you are not currently taking medication for constipation, you will be given a supply of macrogol by the study doctor and given advice on its use.

- Uncommon side effects:

Slight abnormalities in tests of liver function have been reported in less than 1% of people and were not associated with any symptoms. We will be repeating the blood test at the end of 12 weeks treatment, to determine how common this is, and to ensure that any increases are within healthy limits.

There is potential risk that ondansetron treatment may lead to a slight change in your heart rate or rhythm. There have been reports that ondansetron may cause a lack of blood flow getting to your heart muscle meaning that your heart isn't getting enough blood which may cause fatigue and shortness of breath. Although we do not expect this to be significant, we

will be repeating the ECG after 6 weeks treatment, to make sure that any change is within healthy limits before we advise you to continue with the remaining 6 weeks of the study drug.

There is also a potential, although uncommon, risk of movement disorders but current observations have demonstrated that none of these effects are long lasting. Your movement will therefore be monitored during the trial and any worsening of the condition will be clinically managed by your clinician.

17. What are the possible benefits of taking part?

We cannot promise the study will help you, but the study drug may be effective in treating your visual hallucinations. Throughout your participation in the study, you and your caregiver will have the opportunity to work and interact with the research team and other healthcare professionals both at your home and in the clinic. You may find this experience to be helpful for yourself and your spouse, family member, partner or significant other.

The information we obtain from this study will help us understand more about visual hallucinations in people with Parkinson's disease or Lewy Body Dementia. If we find that ondansetron is effective and tolerable as a treatment for visual hallucinations, we will have collected enough information to speed the progression of its use in NHS clinics.

18. What happens when the research study stops?

Once the study has ended your clinical care will continue to be managed by your GP and the local team, which may be led by a neurologist, geriatrician, or a psychiatrist. The research team will not be able to provide further treatment or support. If you continue to experience significant symptoms of hallucination (or other symptoms that need addressing) at the end of treatment, your GP and the relevant specialist will be notified so that you can be referred for further treatment, if necessary.

19. Who can I contact for further information?

You can contact Dr Suzanne Reeves, who is the Chief Investigator of the study, if you have any questions or require any further information about this study. Her details are

Suzanne.reeves@ucl.ac.uk. You may also contact Olga Zubko, Trial Manager for TOP HAT, on o.zubko@ucl.ac.uk

20. What if there is a problem?

If there is a problem or if you have any concerns about the way you have been approached or treated during this study, then please contact: [insert local PI details here]

21. Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

Contact Details

Your Doctor

Name add name Tel. Number: add Tel. number

Your Research/Specialist Nurse/Research Fellow *delete as appropriate*

Name add name Tel. Number: add Tel. number

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

22. What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, we will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, we will make arrangements for your care to continue.

If you decide to continue in the study, we will ask you to sign an updated consent form. If the study is stopped for any other reason, we will tell you why and arrange your continuing care.

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

If you don't want to carry on with the study, you will be free to withdraw from it at any time, without having to give a reason. Withdrawing from the study will not affect the standard of care you receive or your future medical care or legal rights.

If you wish to withdraw from the study, we will ask if you are happy for us to contact you for a brief ten minute telephone call at the 12 week time point, to discuss your hallucinations. This information will ensure we can accurately compare those who received drug and placebo. If you were to withdraw from the study, then we would use any information collected in the study up to the point that you withdrew from the study.

24.What if there is a problem?

If you have any problems, concerns, complaints or other questions about the study, you should contact the local research team (local number), who will try to resolve your problem.

Alternatively, if you feel uncomfortable about doing so, for example if your concerns relate to the local research, please contact the trial manager (Olga Zubko, o.zubko@ucl.ac.uk). She will try to address any concerns and will also guide you in the process of making a complaint if you wish to do so.

Every care will be taken in the course of this clinical trial. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor's (University College London) or the hospital's negligence, then you may be able to claim compensation.

After discussing with your study doctor, please make the claim in writing to Suzanne Reeves (suzanne.reeves@ucl.ac.uk), who is the Chief Investigator for clinical trial and is based at University College London. She will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

You may also be able to claim compensation for injury caused by participation in this clinical trial without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your study doctor in the same way as above.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the clinical trial, the normal National Health Service complaints mechanisms via PALS (Patient Advice and Liaison Service) or local Health Boards Complaints Team in Scotland are available to you. Your local hospital will have a PALs office on site, but can also be contacted by telephone: *[Trust to insert Trust PALs/Health Board Complaints Team telephone number]*. Please ask your study doctor if you would like more information on this. Details can also be obtained from the Department of Health website: http://www.dh.gov.uk.

25. Will my taking part in this study be kept confidential?

This section explains how we manage your data in particular data that could identify your participation in this trial. All information collected about you during the study will be kept

strictly confidential and in accordance with the Data Protection Act and the General Data Protection Regulation 2018.

We will need to use information from you, your medical records, and your GP for this research project. This information will include your contact details, your responses to screening questions, results of any clinical examinations, medical history and current medications, ECG and blood tests as well as pen and paper assessments.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Two types of data will be collected from you during this study:

- Personal data:

This will be collected so that staff from the team at your hospital or clinic can contact you throughout your participation in the research and send you the study results if you have asked for this. This information will solely be used to make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. The information will not be passed on to anyone outside your local team, apart from the trial drug distributors, Modepharma and the courier, who will need to know your study number and address to arrange for the study drug to be delivered directly to your home. The companies involved have data privacy rules in place and the data will not be used for any other purposes other than for the arrangement of medication delivery and all information about you will be destroyed after the end of the trial.

Your information will be held securely on paper and electronically under the provisions of the EU General Data Protection Regulation and Data Protection Act 2018. Personal data will be stored at your local NHS Trust for no longer than it is necessary for them to contact you.

- Research data:

This is the information we have collected from you during all the activities you have taken part in as part of the research. Research data is always saved in anonymised form, this means that the information you share cannot be linked to you but will be assigned under a unique identification number. Research data will be kept for up to 25 years so that the information can be verified at a later date if necessary

26. Additional information about data protection:

UCL is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly.

You can find out more about how we use your information at https://www.hra.nhs.uk/information-about-patients and at https://www.ucl.ac.uk/priment/, information-participants#confidentiality/ or http://www.ucl.ac.uk/jro/who-are-we/data-protection.

You can also find more about how we will use your information by asking one of the research team by sending an email to [insert local research team email], or by ringing us on [insert local research team phone number].

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from the local team at your hospital or clinic, and your GP. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. Data from the study will be anonymised and not linked to your identity, and will be uploaded onto a secure web-based storage site, provided by Parkinson's UK.

The results of the study and anonymised data will be available at the end of the study on clinical trials.gov, so that future researchers can benefit from using this data in future studies, to improve treatment and management of people with Parkinson's disease or Lewy Body Dementia who are experiencing hallucinations.

- If you want to complain about how researchers have handled your information, you should contact the research team. If you are not happy after that, you can contact the Data Protection Officer. The UCL data protection officer can be contacted at data-protection@ucl.ac.uk. If you are not happy with their response or believe they are processing your data in a way that is not right or lawful, you can complain to the Information Commissioner's Office (ICO) (www.ico.org.uk or 0303 123 1113).Will the information that is collected be used for other research?

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.

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.

By signing the consent form you agree to this access for the current study and any further research that may be conducted in relation to it, even if you withdraw from the current study.

27. Will my GP be informed of my involvement?

If you decide to take part in the study, with your permission, we will write to your GP and other doctors who may be treating you to inform them of this, and again at the end of your treatment to update them regarding the outcome.

If we are concerned about any of the test results that may emerge during the study, we may also inform your GP.

28.What will happen to any samples I give?

Blood samples will be taken after 6 and 12 weeks treatment with the study drug, to measure blood drug concentrations. This information will be combined with other information collected during the visit to help us to understand which characteristics (such as age) best predict the relationship between dose, blood concentration and any treatment effects or side effects.

The samples will be posted via a secure Royal Mail Safebox to Analytical Services International (St Georges Hospital) where they will be stored in a freezer, in a secure laboratory, until the study ends.

The reason for storing the sample is that we do not wish your doctor to see the results before the end of the study, as they would indicate whether you were taking ondansetron or placebo. The blood sample will be labelled only with your study identification number and will include no personal details.

The samples will be destroyed after blood drug concentrations have been measured. If you withdraw from the trial, we would still like to store the blood sample until the end of the study as it contains useful information. If you do not wish this to happen, we will arrange for your sample(s) to be destroyed. You do not need to give any explanation as to why you have made the decision.

29. What will happen to the results of the research study?

At the end of the study, we will analyse all of your information together with other participants' information. We will then publish our findings in an academic journal and at relevant conferences. We will also send you a summary of these if you request this.

Your information will not be identified in any publication arising from this study. Although we hope that ondansetron will help to reduce hallucinations, until the trial is completed we will not have positive evidence to support its use in people with Parkinson's disease or Lewy Body Dementia who experience hallucinations.

30. Who is organising and funding the research?

This study is funded by Parkinson's UK. The research is being led by Dr Suzanne Reeves who is an Associate Professor at University College London and a Consultant in Islington Care Home Liaison Team. The research is sponsored by University College London, and supported by the Priment clinical trials unit at UCL. None of the doctors will be paid for including you in the study.

31. Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by East of England - Cambridge East Research Ethics Committee.

32. Further information and contact details

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up-to-date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor. If you require any further information or have any concerns while taking part in the study, please contact one of the following people:

Your study Doctor

Name Tel. Number: add Tel. number

Your Research/Specialist Nurse/Research Fellow

Name Tel. Number:

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.