



Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illnesses: The PRINCIPLE Trial

PARTICIPANT INFORMATION LEAFLET

The PRINCIPLE Trial is trying to find new treatments for COVID-19 that that can be used in the community. We hope to find treatments that help people recover quicker without needing to be admitted to hospital. We are inviting you to join this trial because we understand you are currently experiencing symptoms of COVID-19 and have a positive PCR or lateral flow test for COVID-19.

This leaflet gives information about the trial, including its aims, and tells you about the risks and benefits of taking part.

What is the purpose of the trial?

COVID-19

The PRINCIPLE trial is investigating potential treatments for COVID-19 in adults aged 18 and over, who have a positive test for COVID-19 and symptoms of COVID-19 illness.

Most people with COVID-19 are treated in the community. We urgently need to find treatments that are suitable for use in the community.

The Trial

The purpose of this clinical trial is to find treatments that help those suffering with COVID-19 at home and in the community get better quicker and without needing to be treated in hospital. To be able to do this, we aim to test one or more suitable, possible treatments for COVID-19, as soon as they become available.

We are testing treatments that are well known and have been used for many years around the world, and already have a license for use in the UK. We will also assess less familiar treatments which might have beneficial effects for the treatment of COVID-19, but which do not yet have a license for use in the UK.

All of the treatments in the PRINCIPLE trial have been approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA), as well as the Urgent Public Health panel of independent experts. The MHRA regulates the use of all medicines in the UK.

Please see Appendices for treatment specific information and the known common side effects.

Can I take part?

To take part, you need to have had a **positive test** for SARS-Co-V2 infection which was taken in the last 14 days, AND are unwell with symptoms of COVID-19. These symptoms may include, but are not limited to; a high temperature' a new, continuous cough, loss or change to your sense of smell or taste, sore throat, shortness of breath, general feeling of being unwell, muscle pain, diarrhoea, vomiting, fever, and/or cough. Your symptoms must have begun in the last 14 days and still be ongoing.

Do I have to take part?

No, taking part is entirely your choice and voluntary. It is up to you to decide whether to take part in the trial or not. A decision not to take part will not affect the standard of care you receive from the NHS in any way, now or in the future.

In certain circumstances, we are contacting people who may have recently tested positive for COVID-19, and information about this has been provided to the trial by NHS Digital in these unique pandemic circumstances. You have the right to opt out of any future communications from PRINCIPLE should you wish to do so. If you do not wish to receive further communication from the trial, please let us know. PRINCIPLE will not keep your data should you choose not to take part. For more information, please see the General Notice under the Health Service Control of Patient Information Regulations 2002 (COPI): <https://www.gov.uk/government/publications/coronavirus-covid-19-notification-of-data-controllers-to-share-information>. Following expiry of the COPI Notice, we will have permission to gain access to and process patient identifiable information without consent under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002. For more information, visit (<https://www.hra.nhs.uk/about-us/committees-and-services/confidentiality-advisory-group/guidance-confidentiality-advisory-group-applicants/health-service-control-patient-information-regulations-2002-regulation-5-decision-procedure-research-applications/>). We will make a maximum of three attempts to contact you about the trial.

What will happen to me if I take part?

If you are interested in taking part, we will ask you to complete a short online form to see if you are eligible. If you do not have internet access or would like to telephone us instead, then you can contact us using the contact details at the end of the document.

Informed Consent

You will be asked to complete a consent form online or by telephone. Instructions on how to fill out the form will be provided, so you will know what to do. You will be able to download and keep a copy of your informed consent form.

Initial Questionnaire

You will then complete some questions about you and how you are feeling. We will also collect some contact details such as your name, email address and telephone number. We will also ask you to provide details of a Trial Partner, if there is someone suitable for this. This could be a relative, spouse, friend or carer, if such a person is available, who we will contact for information about you if we are unable to get hold of you for whatever reason.

Randomisation

The final part of the process will tell you whether you will receive standard care or standard care plus a trial treatment. You will be randomly allocated (like rolling a dice) by our computer system to one of these groups and neither you, your GP or the trial team can decide which group you will be in. It will be decided purely by chance.

Before you are randomised a member of your GP surgery or the trial team will call you to confirm your symptoms are still ongoing. You will then receive an email or phone call to let you know which group you have been allocated to; your GP and the trial team will also receive this email. If we find that you cannot participate, we will let you know by email or phone.

Pregnancy Testing and Contraception

For women of child-bearing potential, for safety reasons, if you are randomised to certain medications for which there is currently no human research among pregnant or lactating women, a urine pregnancy test will be provided with your trial pack. You will need to take the pregnancy test on Day 1 of the trial and confirm a negative test result during a telephone call with the trial team, prior to starting your course of trial treatment. If the pregnancy test is negative you can start your medication and then confirm the result with the trial team when they call you. If you receive a positive test result, you will be asked not to take any of the medication, return it to the trial team, and you will be withdrawn from the trial. The pregnancy test provided must be taken prior to taking your first dose of trial medication. If you receive an invalid test result, please contact the trial team using the contact details at the bottom of this leaflet to request a replacement test kit as soon as possible. If the delay caused by the need to send a replacement test kit causes you to become ineligible for the trial (either because it has been more than 14 days since your positive COVID-19 test result, or you are feeling recovered from your illness), we will need to withdraw you from the trial.

Furthermore, women of childbearing potential, or males with a partner of childbearing potential must be willing to use highly effective contraceptive** for the 28 day duration of the trial.

** The implant, the coil, and male or female sterilisation will be acceptable for participating in the trial. The injection and most forms of hormonal contraception will also be considered acceptable for the trial, if used in combination with condoms or other barrier methods. However, condoms alone won't be sufficient during the trial.

However, if you or your partner do become pregnant during the 28 days of your participation in the trial, you must tell us immediately. We may ask you and your partner to allow us to collect follow-up information about the pregnancy and the health of the baby. Your partner will be provided with a pregnant partner information leaflet and will be asked to sign a consent form to allow the study team to obtain relevant information relating to your partner's pregnancy and birth.

Trial Treatment

If you are randomised to the standard care plus trial treatment group, arrangements will be made for the medication to be delivered to you. You will also receive instructions on how to take it and for how long, and you will be asked to confirm receipt of the medication via telephone call. Should your condition worsen at any time during the trial, you should not contact the trial team about this, but contact your GP or other usual services that are open to you.

Follow-Up

You will receive a text message from us to ask you to complete online questions relating to your symptoms and how well you feel every day for up to 28 days after you start the trial. If the trial team don't receive your daily diary answers online, they will text or telephone you on day 7, day 14 and day 28 of the follow up period and ask you a brief set of questions over the phone. There will be a maximum of three attempts to you for each follow-up time point, and if we are unable to contact you we will contact your trial partner – if provided.

Some of the treatments we are testing in the study may not be licensed for use in the UK. We call these 'less well known treatments'. If you have been allocated to receive a less well known treatment, a member of our trial team will contact you within one day of joining the trial, as well as on Day 3. During the Day 1 call, a doctor or nurse will check you are still happy to take part in the study and explain specific side-effects. On Day 3, we will confirm that you have received your participant pack, and read and understood the medication card provided. Please see the Patient Information Sheet appendices for further details about the trial treatments and those classed as less well known. You will also be able to call us at any time if you have any concerns about side effects caused by the treatment, using the trial freephone number: **0800 138 0880**. If you are allocated to a less well known treatment and report any major side-effects (those that cause considerable limitation in your usual activity, require medication or medical attention), and we are unable to contact you or your study partner, with your consent we will contact your GP directly. We will ask you to return any unused medication in a pre-paid envelope to the trial team, via courier.



Following the 28-day study period, we will contact you (via email and/or telephone call) for longer term follow-up questionnaires after your 3, 6, and 12 months (within 3 month of the time points) on the study to collect information about ongoing symptoms, hospital visits, and your well-being. In addition, we will collect information from your GP records and data held by central NHS bodies (such as NHS Digital) for long-term follow-up for up to 10 years, to help us better understand the long-term effects of COVID-19 and the trial treatments.

Supporting other COVID-19 trials

Our main aim is to find treatments that can be used in the community and that are effective against COVID-19. We are working with other researchers to achieve this. You may receive information about other treatment trials from the PRINCIPLE trial platform.

What happens if I am admitted to Hospital?

It is really important that we know if you are admitted to hospital at any point during the 28 day daily follow up period. We need to know about this whether or not you are taking the trial medication. We will give you a card that you can carry to let other healthcare professionals know that you are taking part in this trial. It is also really important that someone close to you knows that you are taking part in the trial, so that if you do get admitted to hospital, they can use the details on the card to let us know.

We may also access your medical records and data held about you in central NHS registries and databases (including NHS Digital, UK Health Security Agency (UKHSA), other equivalent bodies, and genetic or other research databases if you have provided samples to them) to collect information on any hospital admission that you may have during the follow up period.

Optional Follow-up

We are planning to interview a group of people about their experiences after they finish the main trial. This part of the trial is also optional. You will be able to confirm on the consent form whether you are happy to be contacted by the research team about this. If you agree, the research team will contact you with details of the interview after approximately 28 days.

You can then decide whether you want to take part or not.

What are the possible disadvantages or side effects of taking part?

With any medicine, including ones that are already used within the NHS, there is a risk of side effects. Please see Appendices for details of the side-effects common to each drug. You will be asked to tell us if you are experiencing any of these symptoms in your daily diary, or you can contact the trial freephone number. On a daily basis, if you are taking a less well known medication, the trial's clinical team will monitor specific, pre-defined potential side-effects that you report in your daily diaries for the 28 day study period, and contact you if required. Please see the medication specific appendices for details about which side-effects will be monitored for each treatment.

What are the possible benefits of taking part?

We do not know if the treatments being tested will have additional benefits. Your trial treatment may, or may not, help you personally, but this trial should help future patients.

What will happen if I do not want to continue with the trial?

If you decide to take part, you can still withdraw at any time without giving a reason. Information collected up to that point will still be used. If you have informed the trial team of certain moderate or major side effects from taking a trial medicine not licenced in the UK, the trial team would like to contact you and/or your GP until you feel better.

If you wish to withdraw from the trial, please contact the trial team using the contact details at the end of this document. The decision to withdraw will not affect the standard of care you receive from the NHS in any way, now or in the future.

Expenses and Payments

You will be reimbursed for your participation through gift vouchers worth a total of £20. You will receive the voucher at the end of your follow up period, once we have received your completed symptom diary and you have returned any unused medication to the trial team.

What if there are any problems?

If you have any questions about this trial, please contact the Trial Team (See the last page for contact details).

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this trial, you should contact the trial team on principle@phc.ox.ac.uk or **0800 138 0880** or you may contact the University of Oxford Research Governance, Ethics and Assurance Team (RGEA) office on 01865 616480, or the head of RGEA, email_ctr_g@admin.ox.ac.uk.

What will happen to my data?

All information about you and your health will be kept private. The only people allowed to look at the information will be the doctors running the trial, the trial team and the regulatory authorities who check that the trial is being carried out correctly. A privacy notice is on the trial website www.principlertrial.org/participants/how-to-join-the-trial#further-information.

As part of the trial enrolment process we may need to view your Summary Care Records (SCR) (<https://digital.nhs.uk/services/summary-care-records-scr/summary-care-records-scr-information-for-patients>) to check your medication, allergies, adverse reactions and 'Additional Information' to make sure that it is safe for you to take trial medication. A SCR is an electronic record of important patient information, created from GP medical records. SCR 'Additional Information' includes information recorded in your GP record about your significant illnesses and health problems, operations and vaccinations you have had in the past, how you would like to be treated (such as where you would prefer to receive care), what support you might need and who should be contacted for more information about you. SCRs can be seen and used by authorised staff in other areas of the health and care system involved in your direct care.

We will ask for your consent to view your SCR. The SCR will not be retained by the trial team. If your SCR is unavailable, you can still take part in the trial as we will obtain this information from your GP.

What if relevant new information becomes available during the trial?

Sometimes during the course of a research project, new information becomes available about the treatment that is studied.

If this happens, the trial team will tell you about it and discuss with you whether you want to continue in the trial or not.

If you decide to continue you may be asked to sign an updated consent form.

What will happen to the results of the trial?

Results will be published in scientific journals, presented at scientific conferences, and published on the Oxford University departmental website, and may be reported in news media. It will not be possible to identify you in any report, publication or presentation. If you would like to receive copies of any publications arising from this trial, please contact the trial team (details are on the last page).

Who is organising and funding the research?

Funding has been provided by UK Research and Innovation (UKRI) and National Institute for Health Research (NIHR). PRINCIPLE has been set up by the Primary Care Clinical Trials Unit at the University of Oxford. In-kind contributions: Department of Health and Social Care and IPS Pharma provided Favipiravir, free of charge.

Who has reviewed the trial?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC). The REC is there to protect your safety, rights, wellbeing and dignity. This trial has been ethically reviewed and was approved by the South Central - Berkshire Research Ethics Committee (REC Reference: 20/SC/0158).

This trial has also received approval from the Medicines and Healthcare products Regulatory Agency (MHRA).

Contact the Trial Team:

Tel. 0800 138 0880

[Email: principle@phc.ox.ac.uk](mailto:principle@phc.ox.ac.uk)