**PRINCIPLE** aims to rapidly evaluate different treatments that could stem the progression of COVID-19 symptoms, and help ease the burden on hospitals. Any healthcare professional can facilitate recruitment into PRINCIPLE, by guiding patients through screening, consent, registration, or by performing an eligibility check, or by sign-posting to the trial.

### Who do we want to recruit?

- **Patients aged 18 years or over**
- **WITH** a positive COVID-19 test *(PCR or Lateral Flow)* within the last 14 days
- **AND** presenting COVID-19 symptoms within the last 14 days

### COVID-19 symptoms include (but not limited to):

- High temperature
- New continuous cough
- Change/loss of smell/taste
- Sore throat
- Shortness of breath
- Muscle pain
- Diarrhoea and vomiting

**AND**

- Not currently admitted to hospital
- Not previously participated in the PRINCIPLE trial

### Exclusion criteria (Favipiravir arm)

- Known or suspected pregnancy
- Breastfeeding during the course of the trial
- Women of childbearing potential (or male with a partner of) not prepared to use highly effective contraception for the duration of follow up in the study
- Known allergy to Favipiravir
- Currently taking Favipiravir
- Known history of gout
- Known severe liver disease

### Exclusion criteria (Ivermectin arm)

- Known allergy to Ivermectin or any of its excipients
- Known or suspected pregnancy
- Breastfeeding during the course of the trial
- Women of childbearing potential (or male with a partner of) not prepared to use highly effective contraception for the duration of the study
- Ever having travelled to countries that are endemic for *Loa loa* (Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Ethiopia, Equatorial, Guinea, Gabon, Republic of Congo, Nigeria and Sudan)
- Known bleeding disorder
- Known severe liver disease
- Currently taking the following drugs: quinidine, amiodarone, diltiazem, spironolactone, verapamil, clarithromycin, erythromycin, itraconazole, ketoconazole, cyclosporine, tacrolimus, sirolimus, indinavir, ritonavir, cobicistat, warfarin
- Consumption of grapefruit juice
### Participant involvement

Participants will complete an online diary for 28 days and will receive an email reminder with a link to the online diary system. They will be asked daily questions about their symptoms, their medication (if applicable), other prescriptions, and contact with healthcare providers (takes approx. 10 mins/day to complete).

- If online diary access is not possible, the trial team will telephone participants on days 7, 14 and 28 to collect this information.
- All participants will receive a Day 1 telephone call from a clinician to discuss the medication they have been randomised to, and a Day 3 call to check that they have received their participant pack via courier.

### Study Partner

To ensure that patients who may be too unwell at home can still register for the trial, a chosen Study Partner (family member, partner etc.) can help by completing trial procedures and to provide information on the participants’ behalf where necessary.

### How to identify the right patient:

- Run a daily report to find those 18 and over with a positive COVID-19 test and contact patients directly.
- The preferred method of contact is via phone, or you can contact via text message from the practice using the approved wording on the PRINCIPLE website (www.principletrial.org/health-professionals/primary-care).

### What to do next:

1. Recruit the patient yourself. Go to [https://www.principletrial.org/participants/how-to-join-the-trial](https://www.principletrial.org/participants/how-to-join-the-trial) and click the ‘screening questionnaire’ button. *N.B you are verbally supporting someone to self-consent to the trial and transcribing this information into the online system. Therefore, GCP training is not required.* OR
2. Refer the patient to the study team: **0800 138 0880**, who will guide the patient through enrolment. OR
3. Refer the patient to **self-enrol**: [https://www.principletrial.org/participants/how-to-join-the-trial](https://www.principletrial.org/participants/how-to-join-the-trial)

### Please notify the trial team of any Serious Adverse Events (SAEs)

Hospitalisation or death **NOT due to COVID-19**, MUST be reported within 24 hours of becoming aware.

### Contact us

Email: principle@phc.ox.ac.uk Tel: 0800 138 0880
Or visit: [https://www.principletrial.org](https://www.principletrial.org)

### Study Partner

GPs providing information to confirm a patient’s eligibility will be reimbursed **£50 per patient**.