Guidance for GPs

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 with any of the following symptoms, within 14 days since onset:

High temperature | New continuous cough | Change/loss of smell/taste | OR a positive COVID-19 test with any symptoms

AND:

- **Aged ≥65 *OR***
- **Aged 50-64 and experiencing a shortness of breath as part of COVID-19 illness *OR***
- **Aged 50-64 with any of the following known co-morbidities:**
  - Weakened immune system due to a serious illness or medication (e.g. chemotherapy)
  - Heart disease and/or hypertension
  - Asthma or lung disease
  - Diabetes
  - Liver disease
  - Stroke or neurological problem
  - Self-reported obesity or body mass index ≥35 kg/m^2
- Not currently admitted to hospital
- Not previously participated in the PRINCIPLE trial

Exclusion criteria (Favipiravir arm)

- Aged <50 years old
- Known or suspected pregnancy, or breastfeeding during the course of the trial
- Women of childbearing potential(and not prepared to use highly effective contraception for the 28 day duration of follow up in the study)
- Known allergy to, or 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
- Women of childbearing potential
- 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

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

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:

i) Recruit the patient yourself. Go to 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***

ii) Refer the patient to the study team: **0800 138 0880**, who will guide the patient through enrolment. ***OR***

iii) Refer the patient to **self-enrol**: https://www.principletrial.org/participants/how-to-join-the-trial

2. Check eligibility, either i) **online** using Sentry (sites only) or ii) **over the phone** with the study clinical team or iii) send a patient **medical summary** to the study clinical team to review.
The study team will contact you to request the information required and let you know how to provide it.

3. Patients will be automatically randomised to receive *either* **usual care or a treatment arm (Favipiravir or Ivermectin)**, and the study team will courier a study pack directly to the participant. The study pack contains a participant ID card, self-swab kit, instructions and return envelope, information booklet, and if applicable the medication and medication instruction card.
**If Clinicians wish to prescribe the trial medication themselves, please let the trial team know via email (principle@phc.ox.ac.uk)*. Please see the protocol for medication doses.*

Participant involvement

Participants will start completing their 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) and contact with healthcare providers (takes approx. 10 mins/day to complete)

- If online access is not possible, the trial team will telephone participants on days 7, 14 and 28 to collect information about how the participant is feeling.
- All participants will be telephoned on Day 3 to check that they have received their participant pack (and medication if applicable) and ask if they have any questions

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.

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.

Contact us

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

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

NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES
Primary Care Clinical Trials Unit
UK Research and Innovation
NHS