**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.

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**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 18-64 and experiencing a shortness of breath as part of COVID-19 illness OR
- Aged 18-64 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/m²
- Not currently admitted to hospital
- Not previously participated in the PRINCIPLE trial

**Exclusion criteria (Colchicine arm)**

- Is pregnant or planning on becoming pregnant during the course of the trial
- Is breastfeeding or planning on starting during the course of the trial
- Is a woman of childbearing potential (pre-menopausal female that is anatomically and physiologically capable of becoming pregnant) and not willing to use a highly effective method of contraception
- Is hypersensitive for any of the following: Colchicine, Lactose, Pre-gelatinised Maize Starch, Stearic Acid, Purified Water, Ethanol (96%)
- Has a known blood disorders that require regular hospital appointments
- Severe renal impairment or required dialysis
- Severe liver disease
- Currently taking the following medication: Clarithromycin, Cobicistat, Colchicine, Cyclosporin, Diltiazem, Disulfiram, Erythromycin, HIV protease inhibitors (e.g. ritonavir, atazanavir), Itraconazole, Ketoconazole, Quinidine, Verapamil, Voriconazole
- Inflammatory bowel disease or chronic diarrhoea

**Exclusion criteria (Favipiravir arm)**

- Aged <50 years old
- Known or suspected pregnancy, or breastfeeding during the course of the trial
- Women of childbearing potential (as described above)
- Known allergy to, or currently taking Favipiravir
- Known history of gout
- Known severe liver disease
How to identify the right patient:

- Run a daily search for patients with a recent positive test for SARS-CoV-2.
- Run a search for all patients who might be eligible if they were to become ill. Download the search from [https://sites.google.com/nihr.ac.uk/it-solutions-tv-sm/study-resources/principle](https://sites.google.com/nihr.ac.uk/it-solutions-tv-sm/study-resources/principle)

**What to do next:**

**i)** 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**

**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](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** (Budesonide or Colchicine if aged 50+, or Colchicine if aged 18-49), 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](mailto: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](https://www.principletrial.org)