Appendix 1- Molnupiravir

Treatment Information

Molnupiravir is an oral (i.e., taken by mouth) antiviral treatment that was initially developed for treatment of influenza. The treatment has been shown to have a good safety profile. In several clinical trials, it has been shown to improve recovery from COVID-19 symptoms and reduce the need to be admitted to hospital and may therefore be an effective treatment for COVID-19.

Molnupiravir has a conditional license, which means that it has been licensed for use as a treatment based on less data than normally required. To receive this license, the data has shown that the treatment's benefits outweigh the risks. The aim of PANORAMIC is to collect more data to confirm whether molnupiravir is an effective COVID-19 treatment.

Molnupiravir Dose and Administration

Molnupiravir is a new possible treatment for COVID-19, so the most effective dose is unknown. Studies like this are trying to find out how well the treatment works.

For this trial, 4 capsules (200 mg) of molnupiravir are to be taken orally twice a day for 5 days.

You can take the 1st dose as soon as the medication arrives as long as you can leave at least a 4 hour gap before the evening dose. For example, the 1st dose can be taken at 5pm and the second dose at 9 pm or later on day 1. If you cannot take the 1st dose before 5 pm or leave a 5 hour gap, take the 1st dose in the evening and the 2nd dose the next morning, 12 hours apart. Then the medication should be continued morning and evening from day 2 onwards.

If you decide that you no longer wish to take the medication, you will be asked to return your medication to the trial team in the pre-paid envelope.

Potential COVID-19 Treatment

Several small clinical studies have found that molnupiravir may help to treat COVID-19. However, we need more evidence from large clinical trials, which is why we have included the treatment in the PANORAMIC Trial. Molnupiravir has been highly recommended by the Antivirals Taskforce (ATF) for the treatment of COVID-19.

The use of molnupiravir in PANORAMIC has been approved by the MHRA. The MHRA regulates the use of all medicines in the UK.

Exclusion Criteria

Before you are enrolled, you will be asked if you meet any of the following reasons for NOT taking molnupiravir. If you meet ANY of the following criteria, you will automatically be excluded from receiving molnupiravir.

Exclusions: If you meet any of the following criteria you should not take molnupiravir:

- Patients currently admitted to hospital (inpatient)
- Previously enrolled in the PANORAMIC trial
- Currently participating in a clinical trial which involves taking a new medication for COVID-19
- Known or suspected pregnancy (confirmed by a negative pregnancy test)
- Breastfeeding
- Participants of childbearing potential who are NOT willing to use effective contraceptive for the 28 day duration of the trial.
- Known allergy to molnupiravir
- Currently taking molnupiravir outside the trial

A registered nurse, pharmacist or doctor will telephone you to discuss these screening questions with you and to check that you can take the treatment. Once confirmed you will be enrolled into the trial.

Participants of childbearing potential must agree to perform a pregnancy test provided by the trial and confirm a negative test result before taking molnupiravir. This negative test result is required regardless of their current contraception methods or relationship status.

Contraception

As there is currently no human research associated with the use of molnupiravir among pregnant or lactating people, it is important that participants of childbearing potential, must use effective contraceptives from enrolment until day 28 of follow-up. Participants of child-bearing age will also be required to confirm a negative pregnancy test (test provided by the trial), prior to starting the medication.

Methods of contraception that are acceptable for use with molnupiravir include the following:

The implant, the coil, male or female sterilisation, the injection, combined hormonal contraception (e.g. “the pill”, patch, vaginal ring) or the progestogen only pill (“the mini-pill”) will be acceptable for

use with molnupiravir. However, condoms alone won't be sufficient during the trial. Being abstinent for the 28 days before enrolling in the trial and continuing to be abstinent for the 28-day duration of follow-up will also be acceptable where this is in line with your preferred and usual lifestyle. You can discuss any questions you have about contraception during the trial period with the trial team.

If you were to become pregnant during the trial you must tell us immediately and you will be withdrawn from the trial, although we will ask to follow you up for safety reasons.

It is important to note that a barrier method on its own is not sufficient.

Side-effects

Common side effects include dizziness, headache, diarrhoea, and nausea.

A trial doctor or research nurse will call you the day after you start your medication (Day 2) to ask about these and any other side-effects you may have experienced. If you experience any side-effects which you're concerned about while taking molnupiravir, you will be given access to a 24-hour telephone line to speak to a member of the clinical team. Any symptoms reported in your daily diary are monitored by our clinical team who will call you if there any symptoms of concern.

Emergencies

If a medical emergency related to your treatment for this trial occurs while you are at home, you should initially try to contact the usual services that are open to you, such as 111, 999 or go to the accident and emergency (A&E) department at your local hospital. If you are unable to get to the hospital you should contact your GP who, with your consent, will already have been informed of your participation in the trial. You have been given a PANORAMIC participant card that you must show to the doctor you see.