

Appendix 1 Inclusion/Exclusion Criteria

Inclusion Criteria

Patients will be invited to participate in the study if they meet all of the following criteria:

1. Aged between 18 and 64 years (inclusive)
2. Fulfil the DSM-IV criteria practice for schizophrenia or schizoaffective disorder, based on the Diagnostic Interview for Psychosis (DIP)
3. Have received oral clozapine for a period of no more than 2 weeks
4. Agree to participate, have capacity to consent and are able to follow the study instructions and procedures
5. Fasting Blood Glucose Level ≤ 6.0 mmols (confirmed within the previous two weeks of commencing clozapine)
6. BMI ≥ 18 and ≤ 40

Exclusion Criteria

Patients will be excluded from the study if they meet any one of the following criteria:

1. Known allergies to Metformin or any part of the formulation of the investigational product
2. Obesity induced by other endocrinologic disorder (e.g Cushing Syndrome, Hypothyroidism)
3. Current use of any weight-lowering therapy including: pramlintide, sibutramine, orlistat, zonisamide, topiramate or phentermine (either by prescription or as part of a clinical trial)
4. Diagnosis of Type 1 or Type 2 Diabetes mellitus or already on metformin
5. Participants treated with corticosteroids or other hormone therapy (except oestrogens or thyroxine) for greater than 10 days (as they may lead to change in weight)
6. Chronic kidney disease (eGFR < 60 mL/min)
7. Previous surgical treatment of obesity
8. BMI ≤ 18 or BMI ≥ 40
9. Any concomitant disease or condition that according to the investigator's assessment makes the patients unsuitable for trial participation
10. People who are unable to understand or communicate in English
11. For female participants, those currently pregnant, or planning to become pregnant or lactating or no acceptance to the use of effective contraception during the study period
12. Inability to follow the study instructions and procedures

Appendix 2 SAE

Definition of a Serious Adverse Event (SAE)

A serious adverse event is any untoward medical occurrence that, at any dose:

- a) results in death
- b) is life threatening*
- c) requires in-patient **hospitalisation or prolongation of an existing hospitalisation. Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
- d) results in disability/incapacity, or
- e) is a congenital abnormality / birth defect.
- f) Any event deemed by the investigator as being a significant medical event.

*The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/reaction which hypothetically might have caused death if it were more severe

** The term "hospitalisation" is the definition of a subject admitted to a hospital/inpatient (irrespective of the duration of physical stay), or not admitted to a hospital/not inpatient, but stays at the hospital for treatment or observation for more than 24 hours. Hospitalisations for administrative, trial related and social purposes do not constitute AEs and should therefore neither be reported as AEs or SAEs. Likewise, hospital admissions for surgical procedures planned prior to trial inclusion are not considered AEs or SAEs.

Appendix 3 Withdrawal Criteria

Participant Withdrawal by the Investigator

Participants will be withdrawn from the study by the Investigator, prior to completion of treatment, under the following conditions:

- Non-adherence with study medication for seven or more consecutive days
- Non-adherence with or self-ceased clozapine for 7 or more consecutive days
- Non-adherence of more than 50% of study medication on pill count.
- Clozapine ceased due to medical reasons with no planned re-challenge within 7 days of ceasing
- Development of a serious adverse event assumed to be associated with the study medication
- Cessation of effective contraception or confirmed pregnancy
- Development of T2DM
- Continual inability to provide informed consent