Study Title: Single-dose oral bioequivalence study of Primaquine 15 mg tablet (test product) and Primaquine 15 mg tablet (reference product) in healthy adult human subjects under fasting conditions.

Short title: Primaquine bioequivalence study **(**PBE)

Phase of the trial: Bioequivalence

CTA Number: ET-CT-0041

Protocol No. MAL21009

Version No.4.0 **Date:** June 14, 2023

National Principal Investigator (NPI): Mekonnen Teferi

Trial Site: Armauer Hansen Research Institute (AHRI) BE/Pharmacology unit

Sponsor: The Masters & Scholars of the University of Oxford

Ethics Approval date: August 10, 2023

Submission Date to EFDA: October 19, 2023

EFDA Status of trial (Approval or Rejection): Approved **Date:** June 5, 2024

Study Rationale

WHO prequalification offers the possibility of a line extension based on demonstrating proportionality with the adult 15 mg tablet. For a generic manufacturer, a bioequivalence study must be performed comparing the generic (test) product with the reference 15 mg of primaquine. This study is to establish the bioequivalence of a new scored 15 mg generic PQ tablet, produced by IPCA in India.

General objective / Study aims

To compare and evaluate the oral bioavailability of the Primaquine 15 mg tablet of IPCA with that of the Primaquine 15 mg tablet of Sanofi in healthy, adult human subjects under fasting conditions and to assess tolerability.

Primary objectives

Objective: To compare and evaluate the oral bioavailability of the Primaquine 15 mg tablet of IPCA with that of the Primaquine 15 mg tablet of Sanofi in healthy, adult human subjects under fasting conditions.

Outcome measures

- Cmax
- AUCt

Secondary Objectives and Outcome Measures

Objective: Assess tolerability of PQ

Outcome measures:

- AUCi, Tmax, Kel, AUC_%Extrap_obs, tHalf
- Detection of clinical and laboratory adverse events

Study Design

An open-label, randomized, two-period, two-treatment, two-sequence, crossover, balanced, single-dose oral bioequivalence study

Study Population

Healthy individuals

Eligibility Criteria

Inclusion Criteria:

- Age between 18 and 55 years old
- Male and non-pregnant, non-lactating female
- BMI between 18.5 and 30.0 kg/m2
- Able to communicate effectively with study personnel
- Willing to provide written informed consent to participate in the study
- Non-smokers
- All volunteers must be judged by the principal or sub-investigator or physician as normal and healthy during a pre-study safety assessment.

Exclusion criteria:

- History of allergic responses to Primaquine or its formulation ingredients.
- Clinically significant abnormal findings during screening
- Any disease like diabetes, psychosis or others
- History of bronchial asthma
- Use of any hormone replacement therapy within 3 months
- A depot injection or implant of any drug within 3 months
- Use of CYP enzyme inhibitors or inducers within 30 days
- History or evidence of drug dependence or of alcoholism
- History of difficulty with donating blood or accessibility of veins.
- A positive hepatitis, HIV, and Syphilis
- Volunteers who have received a known investigational drug
- Volunteers who have donated or lost blood
- History of difficulty in swallowing or of any gastrointestinal disease
- Intolerance to venepuncture
- Any food allergy, intolerance, restriction or special diet
- Institutionalized volunteers.
- Use of any prescribed, OTC products, vitamins and herbal products
- Use of grapefruit and grapefruit-containing products
- Ingestion of any caffeine or xanthine products,
- Ingestion of any unusual diet, for whatever reason
- G6PD deficiency
- Malaria or a significant febrile illness
- History of haemolysis for any reason
- Blood transfusion in within 3 months
- Laboratory test deviation of more than +/-10%
- Renal impairment (eGFR < 90 mL/min/1.73m2)
- Stool positive for ova, cysts or parasites
- Use of herbals or drugs known to cause haemolysis in G6PD deficiency within 6 weeks

Study Duration

13 days

Recruitment period

From July 13 to 31, 2024

Investigational Medicinal Product

Formulation: tablets of the test and reference product of Primaquine 15 mg

Dose: Primaquine 15mg

Route of administration: Oral

Other interventions: N/A

Intervention (s)

Oral administration of the test product of Primaquine 15mg, manufactured by IPCA, and the reference Primaquine 15mg manufactured by Sanofi.

Sample size

40 healthy people

Evaluator's Risk/Benefit Assessment:

The participants may not get direct benefit from the study result, but it could help to assess the bioequivalence of the product and could help to ensure the use of the medicine in Ethiopia. Participants may develop side effects of the medicines, which could be minor in most cases.