ISRCTN10221007 https://doi.org/10.1186/ISRCTN10221007

A study to compare how the body takes in and gets rid of sefaxersen when given by an injection device or a regular syringe in healthy adults

Submission date
13/05/2025

Recruitment status
Recruiting

Registration date
10/09/2025

Overall study status
Ongoing

Last Edited
10/09/2025

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Sefaxersen, the study drug, is currently being investigated in another ongoing clinical study as a possible new treatment for people with a kidney disease called primary immunoglobulin A nephropathy. Sefaxersen is designed to be specifically taken up into liver cells, limiting the drug from being taken into other tissues. Sefaxersen might reduce inflammatory damage to kidneys in patients with primary IgA nephropathy by lowering the activation of inflammatory components made in the liver. Currently, sefaxersen is being given to people as an injection under the skin (subcutaneously) using a vial and syringe. However, a new method called an injection device has been developed to inject the drug.

The purpose of this study is to see if the injection device can deliver the drug just as well as the vial and syringe, while making it easier to do so. More specifically, the study will evaluate how quickly and how much drug the injection device and the vial/syringe deliver into the bloodstream (called "bioequivalence"). It is hoped that the injection device will make it easier to give sefaxersen subcutaneously.

The study will also compare the safety of sefaxersen and how well it is tolerated using both delivery methods.

As sefaxersen is in the early stages of development, trialling it first in healthy volunteers allows researchers to make sure the drug is safe before testing it in vulnerable people and understand the effects of the drug/device/delivery method without the interference of existing health conditions.

Who can participate?
Participants will be selected by the Medicines Evaluation Unit (MEU) after being assessed and tested.

What does the study involve?
The study duration is approximately 28 weeks, including a 5-day stay in the unit where they will be randomised and dosed, followed by 6 follow-up visits. Some of the assessments and tests undergone by participants in the visits include physical examination, blood and urine samples.

What are the possible benefits and risks of participating?
Benefits:
There are no direct benefits to participants through participation in this study.
Risks:
Study medications - As with all medications, the study drug could cause some side effects as detailed in PIS-ICF. Each person reacts differently to a new medication and the participants may experience some or none of the known side effects; Furthermore participants could experience side effects that are not known at this time. The participants will be closely monitored throughout the study for any side effects or unusual symptoms that could be related to the study drug.
Studies evaluating possible side effects of Sefaxersen and how often they occur are still ongoing. Possible side effects that may be caused by similar drugs of the same type include:
Infections: Due to sefaxersen's effect on calming down the immune system, possible risks include increased risk of infections, such as meningitis or bacterial pneumonia.
Liver effects: Some people experienced slightly raised levels of substances in the blood that can suggest inflammation of the liver.
Reduction in platelet count: While these symptoms have not been observed with sefaxersen, in other drugs of the same class, effects have generally been mild and reversible, but in longer-term studies with higher doses, some people were hospitalised for observation and treatment with corticosteroids.
Kidney effects: While most studies, so far, have not produced undesired effects on the kidneys, in some studies, some people have experienced kidney impairment.
Other side effects: General side effects have been seen in small numbers, such as headache, nausea, diarrhoea, constipation, lethargy (lack of energy), runny or bunged up nose, cough, and rash.
Study Procedures - There are also risks from study procedures
Injection site reactions: These are common for medications that are injected subcutaneously.
Electrocardiogram (ECG): Some areas where the sticky pads are placed may need to be shaved, and the pads may cause some pain when removed.
Vaccinations: Mild side effects from vaccination can include redness or soreness at the injection site, muscle or joint pain, headache, fever, nausea, diarrhea, loss of appetite, fatigue and irritability. Some people may feel anxious or faint due to the stress of the needle injection. Very rarely, a severe allergic reaction may occur.
Blood samples: Taking blood may cause discomfort, bruising and, very rarely, infection at the site where the skin is punctured by the needle. Participants may also experience dizziness, nausea or fainting when blood is taken.
Participation in the study may also involve unanticipated risks.
Potential Risks Associated with Pregnancy
There are no research studies that have given reliable evidence of the effect of sefaxersen in pregnant women. Animal studies have not shown any harmful effects directly or indirectly to unborn young. However, exposure to sefaxersen could cause harm to an unborn child.
Participants who are able to get pregnant in the study must use birth control (contraception) to avoid exposing an unborn child to the study drug.
All known risks and side effects are detailed in the PIS to ensure the participant is fully informed before deciding whether to take part in the study. Any new information learned that might change whether participants want to be in this study, will be communicated to participants right away. Participants can decide whether or not to stay in this study at any time. Participants may

be asked to sign a new consent form that says they know about the new information and that they agree to stay in the study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (Switzerland)

When is the study starting and how long is it expected to run for?
May 2025 to August 2027

Who is funding the study?
F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact?
Dr Sarah Casey, scasey@meu.org.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1011906

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
BA45871

Study information

Scientific Title

A randomized, open-label, single-dose, parallel-group study to investigate the bioequivalence of sefaxersen in healthy adult participants following subcutaneous administration via an injection device or vial and syringe

Study objectives
Primary objectives:
To evaluate the bioequivalence of a single 70 mg SC injection of sefaxersen administered using an injection device compared with a vial and syringe.

Secondary objectives:
1. To evaluate the PK of a single 70 mg SC injection of sefaxersen administered using an injection device compared with a vial and syringe.
2. To assess the safety and tolerability of a single 70 mg SC injection of sefaxersen administered using an injection device compared with a vial and syringe.
3. To evaluate the PD comparability of a single 70 mg SC injection of sefaxersen administered using an injection device compared with a vial and syringe.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/07/2025, North West – Greater Manchester (GM) Central (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048023; gmcentral.rec@hra.nhs.uk), ref: 25/NW/0081

Study design
Interventional randomized parallel group controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Other

Study type(s)
Safety

Participant information sheet

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
This is a Phase I, randomized, open-label, single-dose, parallel-group study in healthy male andfemale participants.
Participants will be randomized in a 1:1 ratio to receive a single SC dose of sefaxersen, administered either via an injection device (Group 1) or a vial and syringe (Group 2). Within each

treatment group, participants will be further randomized equally (1:1) based on the injection site (abdomen or thigh), forming Cohort 1 (thigh) and Cohort 2 (abdomen).
Randomization will also account for sex and baseline (Day -1) body weight categories to ensure a balanced distribution of demographic characteristics between the two treatment groups. The body weight categories are as follows: low (≥55 to <67 kg), medium (≥67 to <78 kg), and high (≥78 to ≤110 kg). Sex and body weight category will be considered as stratification factors for the randomization.

The study treatments (investigational medicinal products) are:
• Group 1 (Test): 70 mg (0.7 mL) sefaxersen as a single SC injection using an injection device.
• Group 2 (Reference): 70 mg (0.7 mL) sefaxersen as a SC single injection using a vial and syringe.
As it is an open study, IQVIA Bios will generate the randomization list and this will be then shared with the Head of Pharmaceutical from the Clinical unit.

The total duration of study participation for each participant may be up to approximately 28 weeks (from screening through study completion) as follows:
• Screening period: From up to 90 days until 2 days before study treatment administration (Day-2).
• In-clinic period: Day -1 to Day 4.
• Dosing period: Day 1.
• Follow-up period: Ambulatory visits at 8, 15, 29, 57, 85 and 106 days after study treatment administration.

Participants will be admitted to the study site on Day -1 and discharged approximately 72 hours after study treatment administration (Day 4).

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Bioequivalence

Phase
Phase I

Drug/device/biological/vaccine name(s)
Sefaxersen

Primary outcome measure
Geometric mean ratio and 90% CI (injection device vs. vial and syringe) for the primary PK parameters: AUC0-inf and Cmax derived using a non-compartmental method. If AUC0-inf cannot be estimated with sufficient accuracy, AUC0-t will be used instead. From the time of IP administration until end of study.

Secondary outcome measures
From the time of IP administration until end of study:
1. AUC0-t, (AUC0-168h and any other additional partial AUCs if deemed necessary), AUC0-last, AUC%extrap, tmax, CL/F, Vz/F, λz, and t1/2 derived using a non-compartmental method.
2. Incidence and severity (CTCAE grading) of ISRs:
2.1. Incidence, severity, and nature of adverse events and serious adverse events.
2.2. Incidence of abnormal laboratory findings and abnormal vital signs.

2.3. Incidence of abnormal electrocardiogram assessments.
3. Percent change from baseline in plasma complement factor B levels.

Overall study start date
02/05/2025

Completion date
31/08/2027

Eligibility

Key inclusion criteria
1. Able to participate and willing to give written informed consent and to comply with the study restrictions according to International Council for Harmonisation (ICH) and local regulations.
2. Healthy male and female participants, 18 to 55 years of age, inclusive, at the time of signing the Informed Consent Form (ICF).
3. Body mass index (BMI) of 18.5 to 32.0 kg/m², inclusive.
4. Body weight within 55 to 110 kg, inclusive.
5. Male and/or female participants: The reliability of sexual abstinence for enrollment eligibility for male and/or female participants needs to be evaluated in relation to the duration of the clinical study and the preferred, usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, sympto-thermal, or postovulation methods) and withdrawal are not acceptable methods. a) Female participants: Female participants are eligible to participate if not pregnant, not breastfeeding. b) Male participants: no contraception requirements.
6. Vaccination against Neisseria meningitidis <3 years prior to initiation of study treatment. Vaccination must include coverage of serogroups A, C, W, and Y. Vaccination against serogroup B should be administered according to local guidelines and national availability. A participant's vaccination status should be maintained in accordance with the most current local guidelines or standard of care. If vaccination is required during screening, the vaccination must be completed at least 2 weeks prior to administration of sefaxersen.
7. Vaccination against Streptococcus pneumoniae administered within the recommended timeframe according to the most current local guidelines. If vaccination is required during screening, the vaccination must be completed at least 2 weeks prior to administration of sefaxersen.
8. Vaccination against Haemophilus influenzae B according to national vaccination recommendations for patients receiving complement inhibitors. If vaccination is required during screening, the vaccination must be completed at least 2 weeks prior to administration of sefaxersen.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
118

Key exclusion criteria
1. A history of clinically significant gastrointestinal, renal, hepatic, cardiovascular, allergic /immunologic, pulmonary, hematologic, neurologic, psychiatric, metabolic, or endocrine disease or treatment of which might interfere with the conduct of the study or that would, in the opinion of the Investigator, pose an unacceptable risk to the participant in this study including, but not limited to, any major illness within 1 month before the screening examination or any febrile illness within 1 week prior to study treatment administration.
2. History or evidence of any medical conditions potentially altering the absorption, distribution, metabolism, or elimination of drugs as judged by the Investigator (or designee).
3. History or presence of clinically significant ECG abnormalities, QT interval corrected for heart rate using the Fridericia's correction factor (QTcF) >450 ms for male or >470 ms for female participants, or clinically significant cardiovascular disease.
4. History of malignancy within <5 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death (e.g., 5-year overall survival rate >90%), such as adequately treated carcinoma in situ of the cervix, nonmelanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer.
5. History of complement disorder.
6. Systolic blood pressure <90 or ≥140 mmHg and/or diastolic blood pressure <60 or ≥90 mmHg from the average of two measurements performed at least 1 minute apart during screening.
7. Confirmed resting pulse rate >100 beats per minute or <50 beats per minute, at screening.
8. Participants who were exposed within 2 weeks prior to enrollment to an individual who tested positive for severe acute respiratory syndrome coronavirus 2 should be carefully and comprehensively evaluated as per usual medical practice and institutional guidance before enrollment. The Investigator should assess the benefit-risk ratio for each participant.
9. Any clinically significant history of hypersensitivity or allergic reactions, either spontaneous or following drug administration, or exposure to food or environmental agents.
10. History of hypersensitivity to any of the excipients in the formulation of sefaxersen.
11. History of hypersensitivity, or contraindication to, any of the vaccinations required for inclusion to this study (Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae B).
12. Prior treatment with any oligonucleotide or small interfering ribonucleoside.
13. Use of glucocorticoids, complement inhibitors, and other immunosuppressive medications is prohibited within 30 days or within 5 times the elimination half-life, whichever is longer, prior to Day 1.
14. Participation in an investigational medicinal product (IMP) or medical device study within 30 days before study treatment administration or within 5 times the elimination half-life, whichever is longer.
15. Donation of blood or blood products for transfusion over 500 mL or receipt of blood or blood products and/or significant blood loss within 3 months prior to study treatment administration and for the duration of the study.
16. Clinically significant abnormalities (as judged by the Investigator) in laboratory test results (including complete blood count, chemistry panel, and urinalysis).
17. Platelet count < lower limit of normal.
18. Positive result on hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV) 1 and/or 2.

19. Evidence of hepatorenal syndrome and estimated creatinine clearance range <80 mL/min or clinically significant abnormal sodium and potassium levels.
20. Any suspicion or history of alcohol abuse and/or any history or suspicion of regular consumption/addiction of drugs of abuse within 6 months prior to study treatment administration, or a positive alcohol or drugs of abuse test at screening, or at Day -1 .
21. Impaired hepatic function as indicated by screening AST or ALT ≥1.1 times the ULN or total bilirubin ≥1.1 times the ULN.
22. Use of tobacco or nicotine-containing products currently or within the past 3 months prior to study treatment administration.
23. Participants with insufficient venous access.
24. Participants who, in the Investigator’s judgment, pose a suicide risk, or any participant with a history of attempted suicide.
25. Participants under judicial supervision, guardianship, or curatorship.
26. Participants who, in the opinion of the Investigator, should not participate in this study.
27. Any abnormal skin conditions or potentially obscuring tattoos, pigmentation, stretch marks, or lesions in the area intended for SC injection (i.e., the abdomen and the thigh).
28. Participants who are unwilling to refrain from ingesting caffeine- or xanthine-containing products (e.g., coffee, tea, cola drinks, and chocolate) from admission (Day -1) until the end of the in-clinic period.

Date of first enrolment
29/07/2025

Date of final enrolment
12/12/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Medicines Unit Evaluation (MEU)
The Langley Building, Southmoor Road
Manchester
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M23 9QZ

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Submission to regulatory authorities
The Sponsor complies with the principle of study participants' right to privacy. Throughout this study, participant data will be identified only by a unique identification number. Authorised personnel of the Sponsor, including, without limitation, study monitors, auditors, and other relevant parties, and relevant health regulatory agencies will have direct access to personal medical data to ensure a high-quality standard for the study.

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement

IPD sharing plan summary

Not expected to be made available