A post-market clinical follow-up investigation in healthy volunteers measuring eye parameters to verify performance and safety of Previct® Drugs for monitoring of patients in treatment of substance use disorder

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Primary Objective• P1. Verify if self-administered eye scanning using a smartphone application, using native key features (alone or in predefined combination(s)), can indicate use of each medicinal product (D1-D2).Secondary Objectives• S1. Verify if...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57044

Source
ToetsingOnline

Brief title
Eye monitoring of substance use disorder

Condition

- Other condition

Synonym
addiction, Substance use disorder (SUD)

Health condition

Substance use disorder (SUD)

Research involving
Human

Sponsors and support

Primary sponsor: Kontigo Care AB
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Drug detection, Eye parameters, Medical device

Outcome measures

Primary outcome

Primary Endpoint

P1. For each medicinal product (D1-D2), changes for each subject in key features (alone or in predefined combination(s)) between baseline at visit 2 and under the influence of D1-D2 at LC-MS/MS defined peak concentration, using native key features.

Secondary outcome

Secondary Endpoints

S1. For each medicinal product (D1-D2), changes for each subject in key features (alone or in predefined combination(s) as described in the primary endpoint, see SAP), between baseline at visit 2 and under the influence of D1-D2 at LC-MS/MS defined peak concentration, using refined key features.

S2. For each medicinal product (D1-D2), changes in refined key features alone or in predefined combination(s), between baseline and under the influence of D1-D2 at 10 min and up to 7 h after medicinal product administration. The

comparison is only made using the 5 key features with the lowest p-values from S1.

S3. For each subject, differences between refined key features taken at the clinic (baseline visit 2) and measurements taken in home environment under similar light conditions. This will be performed only with Dbase, Dcon, MCA, MCV. Two different ambient light conditions, as measured with the smartphones, will be compared for dimmed (20-119 Lux) and bright (120-500 Lux) light.

S4. For each medicinal product (D1-D2), differences between refined key features (for the 5 key features with lowest p-value as found in S1, or in predefined combination(s)) observed for the cohort collected under the influence of D1-D2 at peak LC-MS/MS defined peak concentration, and observations collected for the cohort when drug naive (baseline visit 2). In this analysis data will be analyzed at group level (drug influenced and drug naive) without using intra-individual changes. (Hence, the groups are handled as two independent cohorts).

Safety Endpoint

The incidence and severity of adverse events associated with Previct Drugs.

Study description

Background summary

Previct Drugs is a CE-marked eHealth system developed by the Kontigo Care AB intended to be used in treatment of substance use disorder (SUD) to support and monitor patients' treatment at a distance. Previct Drugs is a standalone medical device software classified as a class I medical device according to the Medical Device Regulation (EU) (MDR) 2017/745. Previct Drugs eye scanning function is implemented in a smartphone application (app), which uses the smartphone*s camera to record videos of the pupil and eye movement, and the resulting data is processed to indicate drug usage. Previct Drugs is thereby a portable device easily used by the user in the home environment.

Previct Drugs is one of the devices developed by Kontigo Care AB that belongs to the Previct platform. The Previct platform consists of two CE-marked devices; Previct Alcohol to be used within treatment and monitoring of alcohol and Previct Drugs to be used within treatment and monitoring of SUD.

This investigation is designed as a PMCF investigation to collect additional clinical data to verify the performance and safety of Previct Drugs and enhance the already existing models for indicating the use of cannabinoids and phenethylamines. Previct Drugs will in this investigation be used in accordance with the CE-mark. The results from two previous pre-market clinical investigations, KCClin01 and KCClin02, showed that opioids, phenethylamines, benzodiazepines, and cannabinoids can be detected with Previct Drugs using smartphone-based eye scanning (SES). The results were based on administration of four medicinal products mimicking the use of illicit drugs: Oxycodone (opioid), Lisdexamphetamine (phenethylamine), Lorazepam (benzodiazepine), and Bedrocan (cannabinoid). The dosing of the medicinal products used resembled to a therapeutic dose used in clinic for treatment of diseases. The models were excellent (AUC= ~0.9) for indicating the use of opioids and benzodiazepines, i.e., clinical dosing was high enough. For phenethylamines the models were acceptable (AUC = ~0.7-0.8). For cannabinoids the effect was statistically significant but due to too low dosing giving low plasma concentrations, they did not properly depict illicit drugs use as the abused doses for cannabinoids are much higher than the therapeutic doses. Therefore, this investigation aims to collect additional data for verifying the performance and safety of Previct Drugs under intake of cannabinoids and phenethylamines. The doses to be used in a controlled single administration in this investigation will be increased compared to the KCClin01 investigation, but still correspond with previously safely used dosing in clinical investigations.

The drug intake will in this PMCF investigation be simulated through collecting SES data using Previct Drugs before and after a controlled single administration of commonly used medicinal products from the following classes of drugs: phenethylamines (D1) and cannabinoids (D2). For making this possible, a healthy volunteer population has been suggested as the most appropriate investigation population for being able to collect clinical data before and after the single application of the medicinal product. The population will consist of 30 healthy volunteers (12 for phenethylamines and 18 for

cannabinoids) recruited in the Netherlands. Each subject will participate in the investigation for approximately 7-10 days after the baseline and screening visit.

Study objective

Primary Objective
• P1. Verify if self-administered eye scanning using a smartphone application, using native key features (alone or in predefined combination(s)), can indicate use of each medicinal product (D1-D2).

Secondary Objectives
• S1. Verify if self-administered eye scanning using a smartphone application, after refinement of the method for establishing key features (alone or in predefined combination(s)), can indicate the use of each medicinal product (D1-D2).
• S2. Evaluate the first and last time after medicine intake of D1 or D2 when refined key eye features, alone or in predefined combination(s), differ from baseline.
• S3. Evaluate the difference between refined drug naïve test data collected at the clinic and compared with tests performed in home environment.
• S4 Evaluate if the refined drug naïve key features (alone or in predefined combination(s)), collected at baseline differs from data collected at peak plasma concentration under the influence of D1-D2 without compensating for intra-individual variation.

Safety objective
Verify the safety of using the smartphone application Previct Drugs for collecting self-administered eye scanning data.

Study design

This is a post-market clinical follow-up (PMCF) investigation designed to collect additional clinical data on Previct Drugs to verify its performance and safety, and to improve its drug identification capacity with self-administered smartphone-based eye scanning (SES). The clinical data collected in this clinical investigation is an important step to verify and improve the developed algorithms of the CE-marked system, and to improve the mathematical models for indicating the use of cannabinoids and phenethylamines.

The design of this third clinical investigation KCClin03 is similar to the previously conducted pre-market clinical investigation KCClin01, where the eyes of healthy volunteers were monitored with Previct Drugs before and after intake of one out of four medicinal products (opioids, benzodiazepines, phenethylamines, or cannabinoids). Also, in this investigation will therapeutically used medicinal products be used during a controlled single

administration where Previct Drugs will be used before and after the intake. The substances that will be used are: phenethylamines (30 mg Dexamphetamine - D1) and cannabinoids (Bedrocan (100 mg, containing 22% tetrahydrocannabinol (THC) - D2)). The dosing will be increased with approximately 50% in this investigation compared to KCClin01 to ensure higher plasma concentrations and stronger eye scanning responses compared to KCClin01, and thus a better ability to mimic illicit substance use. This investigation will also use Dexamphetamine instead of Lisdexamphetamine that was used in the KCClin01 investigation due to that Dexamphetamine has a faster Tmax (peaks at 1.5h) compared to Lisdeaxamphetamine that is a slow-release formulation. In total will 20 key features be analysed with Previct Drugs of which seven are new key features to estimate nystagmus and eyelid movements.

Previct Drugs is a CE-marked eHealth system composed of an app and a careportal, intended to be used in treatment of substance use disorder (SUD) to support and monitor patients* treatment. The app is used by patients to perform drug sobriety tests using eye-scanning and report on assigned tasks as defined by the individual treatment plan. The drug sobriety test relies on the analysis of the eye*s reaction on intake of drug substances and gives an indication of the following substances: opioids, benzodiazepines, central stimulants (e.g., amphetamine and other phenethylamines). The test may also indicate intake of high doses of cannabinoids and alcohol. The careportal is used by healthcare professionals to create individual treatment plans and to receive the results on the patient*s treatment adherence and drug sobriety progress.
This investigation will use Previct Drugs per current CE-mark, but there will be some minor differences as some modules/functionalities are not applicable to be used per investigation design and that the study population consists of healthy volunteers which is not the target population of Previct Drugs. Although, the usage and performance of Previct Drugs is the same and therefore it is being used as per CE-mark. The minor differences are:
• The Previct Drugs app will have the following functionality deactivated to enable the clinical investigation to be performed:
- Instead of displaying information on drug intake, a message will be displayed in the app after performing a text, *Thank you for your test*.
- The calibration step will be omitted.
- Follow-up steps, if indication of drugs has been identified will be omitted. These steps are not required based on that the population in this investigation will be healthy volunteers.
• The careportal will be used for providing a subject access to the app and registration of the used smartphone*s identity. The sponsor Kontigo Care will administrate this. The careportal*s functionality and modules normally used by the caregiver will not be available and used in this clinical investigation.
• An external computer will be used for the analysis of the collected data from the app. The external computer/analysis will be handled by the sponsor, Kontigo Care.
• A healthy volunteer population will be used instead of the target population of Previct Drugs to be able to collect data before and after administration of

a medicinal product. The population enrolled will be as per eligibility criteria and thereby within the age limitation of Previct Drugs.

The investigation will enroll and follow-up adult male and female healthy volunteers, i.e., subjects, for collection of baseline data during one week in the subject*s home environment and thereafter performance of a single administration of one of the two medicinal products of interest (D1 and D2) at the site in a controlled setting.

Intervention

Visit 1 at the site:
- Scan they eyes with Previct Drugs 6 times (demonstration and training not included)
- Health examination (e.g., ECG, pulse, blood pressure)
- Urine pregnancy test for fertile female subjects
- Urine test for drug screening
- Questionnaires to be answered by subject

At home between visits 1 and 2:
- Scan the eyes with Previct Drugs 4 times/day (once in the morning, two during the day, and once in the evening) for 1 week (+ 4 days/- 2 days)

Visit 2 at the site:
- Urine pregnancy test for fertile female subjects
- Urine test for drug screening
- Vital signs: oxygen saturation in blood, pulse, blood pressure, temperature
- Scan the eyes with Previct Drugs for 26 times cannabinoids and 28 times for phenethylamines
- Singel administration of the medicinal product
- Collection of blood samples for LC-MS/MS analysis

Telephone follow up
- Confirm safety

Study burden and risks

The risks of using smartphone-based eye scanning through Previct Drugs is very low. Therefore, the main risk of this investigation is related to the administration of the medicinal product, cannabinoids and phenethylamines, and the side effects which they may have. This has been minimized by using a single administration of the medicinal product, that the subjects are under continuous surveillance on the clinic, and the dosing is within used range used for therapeutic purposes. A second risk is dependence, which is considered as very low as during inclusion we exclude all subjects with any kind of psychiatric disorder and addiction tendency, and we use only a single dose of the medicinal

product. The subjects them-self have no direct benefit of the investigation, but it is very common that there is a relative or a friend which have problem with substance use.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Male or female healthy volunteers.
2. Age 18 to 55 years.
3. BMI between 18.5-30 kg/m2.
4. Weight between 50-100 kg.
5. Healthy as determined by the investigator or designee based on pre-investigational medical and surgical history, and health examination at enrollment.
6. Women of childbearing potential (defined as all women who are not surgically

sterile or postmenopausal for at least 1 year prior to enrollment) must have a negative urine pregnancy test at enrollment and at visit 2 and must agree to use a medically acceptable contraception from enrollment until clinical investigation completion.
7. No current drug usage defined as a negative urine drug test at enrollment and at visit 2.
8. Able to use Previct Drugs after initial training (defined as successfully performing a test set after trying maximum three times per measurement).
9. Voluntarily agrees to participate and has duly singed the Informed Consent Form.

Exclusion criteria

1. Participating in another clinical investigation which may affect the clinical investigation outcome according to clinical judgement.
2. Previously participated in the KCClin01 investigation.
3. Pregnant or lactating.
4. Blind and/or deaf.
5. Clinically abnormal ECG, according to the investigator. QTcF time >450 ms at enrollment.
6. Resting heart rate >90 BPM.
7. Current or recent history of alcohol misuse assessed by AUDIT where >=6 points for women or >=8 points for men indicates a potential misuse.
8. Current or history of psychiatric disorder or drug misuse assessed by M.I.N.I where the outcome will be based on clinical judgement.
9. Any disease or condition that may influence pupillary reflexes based on clinical judgement.
10. Undergone eye surgery that may influence pupillary reflexes based on clinical judgement.
11. Ongoing treatment with medications which may interfere with eye measurements based on clinical judgement.
12. Ongoing treatment with medications which may interfere with any of the medicinal products to be used.
13. History or presence of allergy or serious reaction to the medicinal products to be used.
14. History or presence of cardiovascular disease, e.g., arteriosclerosis, hypertension, or cor pulmonale.
15. History or presence of sleep-related breath disorder.
16. History or presence of gastrointestinal disease, e.g., paralytic ileus, acute abdomen, delayed gastric emptying, or chronic constipation.
17. History or presence of pulmonary disease, e.g., acute pulmonary insufficiency, severe respiratory depression with hypoxia, chronic obstructive lung disease, or bronchial asthma.
18. History or presence of autoimmune neuromuscular disease, e.g., myasthenia gravis.

19. Not able to read or understand the local language.
20. Any other condition that as judged by the investigator may make the follow-up or investigation inappropriate.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-11-2024
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Previct Drugs
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	04-10-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-01-2025
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-02-2025
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT06629740
CCMO	NL87202.058.24