An open label study to explore the feasibility and tolerability of 28 days use of intravaginal oxybutynin via the MedRing OAB system in out-patients with overactive bladder

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Primary objective• To explore the feasibility of multiple dose administration of oxybutynin via the MedRing OAB system in an outpatient setting.• Safety and tolerability of 28 days of intravaginal dosing of oxybutynin via the MedRingSecondary...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON56571

Source
ToetsingOnline

Brief title
Feasibility and tolerability of 28 days oxybutynin via the MedRing

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
Overactive bladder

Research involving
Human

Sponsors and support

Primary sponsor: LiGalli B.V.
Source(s) of monetary or material Support: LiGalli B.V.

Intervention

Keyword: Intra-vaginal delivery, MedRing, Oxybutynin, Pharmacokinetics

Outcome measures

Primary outcome

• Questionnaire MedRing OAB system at day 28

- Physical and emotional burden of MedRing system (Q10 to Q24)

- Practical use of MedRing system (Q25 to Q31)

- As needed dosing feasibility (Q32 to Q37)

- General opinion use MedRing (Q38 to Q48)

• Signs and Symptoms:

- Treatment emergent (Serious) Adverse Events ((S)AE) and Device related

(S)AEs

- AE reported via Questionnaire MedRing system Q1 to Q9 on day 2, 7, 14,

21, 28.

• Visual inspection of vaginal mucosae

• Other safety parameters (Vital signs and Lab)

Secondary outcome

• Read out of log data of MedRing on drug delivery and connectivity:

- Dosing time

- Dosing volume

- Temperature

• Synchronization timepoints between MedRing and smartphone App

• Plasma concentrations of oxybutynin and DEOB at day 1, day 14 and day 28.

• Post calibration programmed volume output test

• Questionnaire MedRing OAB system at all timepoints

• Overactive bladder quality of life short-form questionnaire (OAB-q SF) at all

timepoints

• Smartphone app usage:

- Number of openings of the app, adjusting the treatment schedule,

synchronizing between smartphone app and the MedRing.

- Use of reporting, instructions and Frequently Asked Questions

Study description

Background summary

Controlled release technologies, including sustained release of oral medication, implants and transdermal drug delivery, have been developed to mimic physiological concentrations and endogenous substance profiles. The MedRing is an innovative drug delivery device designed for intravaginal drug delivery. The MedRing contains a miniaturized electronic printed circuit board assembly with electronics and antenna, a battery, a drug container, a miniature peristaltic pump, and a temperature sensor; and is loaded with medicinal product. The MedRing can wirelessly connect to a smartphone application (app) from which drug delivery can be programmed and which receives data (dose delivered and temperature) from the ring. The release of drug can be programmed by the physician and has the option of *as needed* control by the patient, within boundaries that are specified remotely by the physician. In both cases, the delivery schedule cannot exceed pre-defined safety limits. A web application to be used in combination with the MedRing and Smartphone app serves as a back-end.

Overactive bladder (OAB) is a common and distressing condition which has a significant effect on quality of life. One of the current treatment options is the competitive muscarine receptor antagonist oxybutynin. However, after oral administration of oxybutynin the anticholinergic side-effects oftentimes

outweigh the advantageous effects, leading to therapy non-adherence. The formation of the metabolite N-desethyloxybutynin (DEOB), which is a result of the extensive first pass effect of oxybutynin, has been linked to the adverse reactions of oral oxybutynin. By administering oxybutynin intravaginally, the first pass metabolism is avoided resulting in a favorable parent/metabolite ratio, which is expected to lead to less side effects. In contrast to intra-vaginal devices in which oxybutynin is released continuously, the MedRing OAB system is developed to administer the compound pulsatile and *as-needed*. This may result in the use of oxybutynin more in line with patients* desires: individual flexible - possibly less - medication, only when needed. Together, the MedRing containing oxybutynin in combination with the Smartphone (also referred to as *Companion App*) and Web application, is referred to as MedRing OAB system.

In a previous study, the safety, tolerability and pharmacokinetic profile of oxybutynin upon an intravaginal single dose via the MedRing in healthy volunteers was assessed (CHDR2032). Additionally, the pharmacokinetic profile of oxybutynin upon administration of multiple intravaginal doses via the MedRing was assessed and compared to oral administration and placebo in healthy volunteers (CHDR2208). A higher parent (oxybutynin) /metabolite (DEOB) ratio was found after intravaginal administration of oxybutynin compared to oral administration. In this study, the safety, tolerability and feasibility of using the MedRing system for the intravaginal delivery of oxybutynin will be explored in patients with OAB in an outpatient setting for 28 days. The feasibility of both a fixed and a flexible dose scheme will be explored, by enabling patients to schedule their dose via a smartphone app.

Study objective

Primary objective
• To explore the feasibility of multiple dose administration of oxybutynin via the MedRing OAB system in an outpatient setting.
• Safety and tolerability of 28 days of intravaginal dosing of oxybutynin via the MedRing

Secondary objective
• To confirm the functioning of the MedRing OAB system during 28 days.
• To assess patient satisfaction and quality of life using the MedRing and the smartphone app for oxybutynin dosing.

Exploratory objective
• Preliminary assessment of clinical effect of oxybutynin delivered via the MedRing OAB system

Study design

This is an exploratory open-label study to assess the feasibility, safety and tolerability of 28 days of intravaginal dosing of oxybutynin via the MedRing and the smartphone app in patients with overactive bladder (OAB) in an outpatient setting.

Intervention

The screening period for this study has a maximum duration of 42 days prior to the insertion of the MedRing. The treatment consists of three treatment periods, with a total duration of 28 days. The intravaginal delivery of oxybutynin via the MedRing system will be performed in three treatment periods.

Treatment period 1 (Day 1 - 14): fixed dosing at fixed timepoints as defined and programmed by the physician. Subjects will receive 3 doses of 2 mg per day (total 6 mg / 24 hours) at preset times.

Treatment period 2 (Day 14 - 21): fixed dosing at flexible timepoints. Subjects will be instructed to administer 3 doses of 2 mg oxybutynin per 24 hours via the MedRing system at free to choose timepoints. The minimum interval between two doses must be 3 hours.

Treatment period 3 (Day 21- Day 28): flexible dosing at flexible timepoints. Subjects will be instructed to administer oxybutynin via the MedRing system as needed. Oxybutynin can be administered in steps of 1 or 2 mg, with a maximum of 6 mg in 24 hours and a minimum dose interval of 3 hours.

Subjects will visit the study site on day 1, 7, 14, 21, 28 and 35. On day 1, subjects will be trained on how to use the MedRing system, including insertion and removal, followed by self-insertion of the MedRing. The first dosing of oxybutynin via the MedRing will be performed at the study site. On day 1, 14 and 28, PK samples will be taken. On day 28, the MedRing will be removed, followed by a vaginal inspection. Final follow-up visit will take place on day 35 +/- 2 days for all subjects participating in the study

Study burden and risks

OAB patients with an indication for oxybutynin treatment will be included. The expected oxybutynin exposures to be reached in the study are within the range of the oxybutynin exposure of the registered oral dose range. Patients will not receive any direct benefit from this study but participation contributes to knowledge on their disease and possibly new treatment options.

The systemic use of oxybutynin in humans is considered safe. Most of the side effects can be explained by the anti-cholinergic mode of action. These side effects are thought to be linked to the metabolite (DEOB), which may be reduced by the intravaginal route of administration circumventing the hepatic

first-pass effect.
Potential issues of concern include:
- Local tolerability issues with the oxybutynin solution or the MedRing to the vaginal cavity.
- Technical malfunction of the MedRing pump system.
- Breakage of the MedRing and releasing the reservoir of oxybutynin intravaginally.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Female subjects, 18 to 80 years of age, inclusive at screening
2. All women of childbearing potential must practice effective contraception during the study and be willing and able to continue contraception for at least

30 days (females) after their last dose of study treatment
3. Patient must have OAB, defined as *urinary urgency, usually with urinary frequency and nocturia, with or without urgency urinary incontinence* according to the guidelines of the ICS/IUGA, diagnosed by a general practitioner or medical specialist
4. Has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions
5. Owns an iPhone or Android smartphone with iOS 15 or higher and/or Android 9 or higher and willing and able to use it during the study

Exclusion criteria

1. Botox injection into the bladder as treatment for OAB within 6 months prior to dosing or percutaneous tibial nerve stimulation (PTNS) within 6 months prior to dosing
2. Active urinary tract infection
3. A vaginal infection or clinically relevant mucosal lesion at vaginal speculum inspection
4. Vaginismus or hypertonia of pelvic floor muscles
5. Being a virgin

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-02-2024
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	MedRing OAB
Registration:	No

Ethics review

Approved WMO Date:	05-02-2024
Application type:	First submission
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
CCMO	NL85570.058.23