The effect of methenamine hippurate to reduce antibiotic prescribing due to new episodes of urinary tract infections (UTI) in elderly women with recurrent UTI- a triple-blinded, randomized placebo-controlled phase IV study

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Primary objective: The primary objective of this study is to investigate if taking methenamine hippurate reduce the need for antibiotic usage due to recurrent UTI (measured as the number of courses of antibiotics).Secondary objectives:to investigate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54960

Source
ToetsingOnline

Brief title
ImpresU WP 3

Condition

- Bacterial infectious disorders
- Urinary tract signs and symptoms

Synonym
cystitis, urinary tract infection

Research involving
Human

Sponsors and support

Primary sponsor: University of Oslo
Source(s) of monetary or material Support: JPIAMR/ ZonMW

Intervention

Keyword: elderly, methenamine, UTI

Outcome measures

Primary outcome

Number of UTI courses during day 2-180 for which antibiotics were prescribed

Secondary outcome

Number of UTI courses in the period up to 6 months after discontinuation of

methenamine

Number of UTI during methenamine

Severity of UTI symptoms

Duration of UTI episodes

Number of complications such as pyelonephritis and hospital admission for UTI

Study description

Background summary

There is a need for a large well-conducted randomised controlled trial (RCT) to clarify both the safety and preventive effect of methenamine hippurate on urinary tract infections for longer term use.

Study objective

Primary objective: The primary objective of this study is to investigate if taking methenamine hippurate reduce the need for antibiotic usage due to

recurrent UTI (measured as the number of courses of antibiotics).

Secondary objectives:
to investigate if methenamine hippurate will have a prolonged effect on antibiotic usage even after discontinuation
to investigate if taking methenamine hippurate reduces the incidence of UTI
to investigate if methenamine hippurate can reduce severity of UTI symptoms
to investigate if methenamine hippurate can reduce duration of UTI episodes
to investigate if number of complications such as pyelonephritis and hospital admission for UTI differ between methenamine hippurate and placebo.

Study design

Blinded randomised controlled phase IV trial where patients are randomised to active intervention (methenamine hippurate) or controls (placebo).

Intervention

Methenamine hippurate vs placebo

Study burden and risks

Potential benefits from IMP:
* decreased total use of UTI antibiotics
* reduced antibiotic pressure on gut microbiota in the population and possibly reduced antimicrobial resistance (AMR) in the population
* decreased number of UTIs
* increased quality of life.
Potential risks from IMP:
* polypharmacy, many patients have a large number of regular medication, and methenamine hippurate will be a new one for six months
* simultaneous intake of sulphonamide antibiotics can increase risk of crystalluria. Therefore methenamine hippurate will temporarily be paused if the participant gets a course of sulphonamide antibiotics . There are no other known clinical relevant interactions between methenamine hippurate and other pharmaceuticals.

Anticipated adverse drug reactions in the study:
Methenamine hippurate is well tolerated and adverse effects are rare and generally mild. Possible side effects might be minor gastrointestinal upsets, dysuria (seldom), abdominal cramps, anorexia, rash and stomatitis. The trial team will be available on telephone for urgent cases during the whole study period.

Risk/benefit rationale:
* The benefit of the study is potentially great for elderly women with

recurrent UTI resulting in fewer UTI episodes, reduced antibiotic usage and therefore also reducing the risk of AMR.
* The risk of the study is considered to be very small.

In summary the benefits greatly outweigh the potential small risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

• woman
• age >= 70 years
• recurrent UTIs defined as >= 3 episodes of antibiotic treated acute cystitis (acute symptoms specific/related to the urinary tract) during the last twelve months or >= 2 episodes during the last 6 months
• able and willing to comply with all trial requirements

• able and willing to give informed consent

Exclusion criteria

• the patient has taken methenamine hippurate within the last 12 months
• the patient is allergic to methenamine hippurate
• the patient is having current antibiotic prophylaxis for UTI
• the patient has a urinary catheter (chronic indwelling catheters as well as intermittent urinary catheterisation)
• the patient has known severe chronic renal failure or estimated creatinine glomerular filtration rate <= 30 ml/min (known = registered in GP* clinical records)
• the patient has a known condition or treatment associated with significant impaired immunity (e.g. long-term oral steroids, chemotherapy, or immune disorder) (known = registered in GP clinical records)
• the patient has a known severe hepatic impairment (known = registered in GP clinical records)
• the patient is suffering from severe dehydration
• the patient has gout
• the patient has a need for long term use of antacids such as magnesium hydroxide, magnesium carbonate, aluminium hydroxide
• the patient has a life expectancy estimated by a clinician to be less than six months
• the patient has been involved in, including completion of, follow-up procedures, in another clinical trial of an investigational medicinal product in the last 90 days
• the patient suffers from incontinence too severe to be able to provide a voided urine specimen
• the patient is participating in ImpresU Work Package 2
• the patient is suffering from significant known abnormal renal tract anatomy/physiology or neuropathic bladder disorders.
• lactose intolerance

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-11-2020
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Hiprex
Generic name:	Methenamine hippurate

Ethics review

Approved WMO Date:	04-03-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-10-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	04-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-12-2021
Application type:	Amendment
Review commission:	METC NedMec

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
EudraCT	EUCTR2018-002235-15-NL
ClinicalTrials.gov	NCT04077580
CCMO	NL71512.041.19