EXtended use of FOsfomycin for the treatment of CYstitis in primary care

No registrations found.

Ethical review	Positive opinion
Status	Suspended
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25501

Source
Nationaal Trial Register

Brief title
EXFOCY

Health condition

uncomplicated cystitis

Sponsors and support

Primary sponsor: UMC Utrecht
Source(s) of monetary or material Support: ZonMw

Intervention

Outcome measures

Primary outcome

Number of days with full resolution of cystitis symptoms within the period of 28 days

Secondary outcome

• Rate of clinical failure within 28 days, irrespective the causing organism

• Rate of microbiological failure at day 28
• Rate of relapses at day 28,
• Rate of reinfections at day 28
• Rate of aggravation to pyelonephritis or urosepsis at day 28
• Rate of hospital admission at day 28
• Rate of mortality at day 28
• Incidence of (severe) adverse events (including fever, diarrhea, nausea, vaginitis, headache, dizziness) on day 7
• Self-reported therapy adherence on day 7
• Satisfaction with the treatment received after 28 days
• The number of days of absenteeism (from payed work or volunteer work)
• Correlation between in vivo and in vitro activity for the investigational treatments

Study description

Background summary

Rationale: Cystitis is the most frequent reason for women to visit their general practitioner. More than 600.000 women suffer from urinary tract infections in The Netherlands each year. Currently, the 1st choice treatment for uncomplicated cystitis is nitrofurantoin (NIT) for 5 days. The second choice is 3 gram fosfomycin-trometamol (FT) in a single dose. FT is increasingly prescribed because it has few side-effects and it has a patient-friendly dosing scheme. Previous research did not show significant difference in efficacy between fosfomycin and nitrofurantoin, but a clinical trial from 2018 claims a single dose of FT might be inferior to 5 days of nitrofurantoin. Pharmacodynamic and pharmacokinetic research suggests that a single dose of FT may be insufficient to cure cystitis. Overall, it remains unknown whether a single gift of FT is as efficacious as 5 days of nitrofurantoin for uncomplicated cystitis with regard to clinical cure and if an additional gift of FT would overcome this. A clinical trial is therefore warranted.

Objective: To investigate the comparative effectiveness and side-effects of 5 days of nitrofurantoin, single dose FT, and extended use of FT in uncomplicated cystitis in primary care.

Study design: An open-label randomized non-inferiority / superiority study with 3 arms.

Study population: 777 non-pregnant women with symptoms of uncomplicated cystitis, with 259 subjects in each study arm.

Intervention: (A) FT in a single dose of 3000mg on day 1; (B) extended dosing of 3000mg FT on day 1 and 3 (C) nitrofurantoin 100mg bid (slow release) for 5 days.
Main study parameters/endpoints: primary: days of absence of cystitis symptoms within 28 days. Secondary: clinical failure on day 28, microbiological failure on day 28, incidence of side-effects, cost-effectiveness

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: A potential risk of participation is that the treatment arm to which the patient is allocated is either less efficacious, has more adverse events or higher recurrence rate than the other treatment arms. However, NIT and FT are both frequently used for urinary tract infections and considered safe and effective compounds for uncomplicated cystitis. According to previous studies, a second dose of FT is well tolerated. The potential risks of participation on severe adverse events is expected to be negligible as the risk of severe clinical failure after cystitis treatment is only 1% according to previous studies and differences between NIT and FT have not been observed previously. A potential benefit of participating to this study is that a more patient friendly treatment scheme is equally effective. For future patients the guidelines could be improved and become more patient-friendly. The burden of participation is considered low. Study participants need to complete a short daily questionnaire on a mobile application up to 28 days.

Study objective

1) Fosfomycin in a single dose is non-inferior to nitrofurantoin
2) Fosfomycin in two dosages on day 1 and 3 is non-inferior to nitrofurantoin
3) Fosfomycin in two dosages on day 1 and 3 is superior to fosfomycin in a single dose

Study design

First participant included in September 2021, study closure September 2024.

Intervention

treatment with fosfomycin-trometamol in a single dose of 3000mg on day 1, and treatment with extended dosing of 3000mg fosfomycin-trometamol on day 1 and 3

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Eligibility criteria

Inclusion criteria

- Adult women (>18 years of age) with a diagnosis of uncomplicated cystitis in primary care
- Cystitis diagnosis is according to the flow diagram in the Dutch NHG-guideline. In line with the NHG guideline 2020, recognition of symptoms should always be accompanied with either a positive nitrite test or leucocyte and dipslide test
- Urine collection is performed according to the Dutch NHG-guideline

Exclusion criteria

- Presence of signs of tissue invasion according to NHG guideline: fever, malaise, chills, flank or perineal pain, signs of sepsis or delirium
- Pregnancy or nursing*
- Diabetes Mellitus
- Immunocompromised state:
o Untreated infection with human immunodeficiency virus (hiv)
o Use of high-dose systemic corticosteroids
o Use of other immunosuppressive medication
- Presence of an indwelling urinary catheter
- History of abnormalities in urinary tract or kidneys
- Neurogenic bladder dysfunction
- UTI in past 28 days before inclusion
- Antibiotic prophylaxis (current or in past 28 days)with nitrofurantoin or fosfomycin or trimethoprim.
- Known GFR <30mL/min
- Contra-indication for nitrofurantoin or fosfomycin use (e.g. allergic reactions, lung or liver reaction or peripheral neuropathy after previous use in clinical history, acute porphyria, G6PD deficiency)
- Current use of an antibiotic for any reason
- Previous inclusion in EXFOCY
- Presence of urine cultures showing resistance for nitrofurantoin or fosfomycin in the last 12 months

Study design

Design

Study type: Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	06-09-2021
Enrollment:	777
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	16-08-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50944
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9706
CCMO	NL75841.041.20
OMON	NL-OMON50944

Study results