# Oral Fosfomycin versus Ciprofloxacin for Febrile Urinary Tract Infection in Men: a pilot study

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To determine the efficacy of oral fosfomycin in comparison to the standard of care oral ciprofloxacin, in the treatment of FUTI after initial empirical treatment with intravenous antibiotics.To describe the pharmokinetic profile of men treated with...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Bacterial infectious disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55825

**Source**
ToetsingOnline

**Brief title**
FOS-MEN

### Condition

- Bacterial infectious disorders
- Urinary tract signs and symptoms

**Synonym**
urinary tract infection

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** HagaZiekenhuis
**Source(s) of monetary or material Support:** Ministerie van OC&W,Subsidie vanuit

wetenschapsfonds HagaZiekenhuis

## Intervention

**Keyword:** E. coli, febrile urinary tract infection, fosfomycin, men, pharmocokinetics

## Outcome measures

### Primary outcome

The primary endpoint is the clinical cure rate (resolution of symptoms) 10 to

18 days post-treatment (= test of cure, TOC).

### Secondary outcome

Secondary endpoints are clinical cure rate during late follow-up (LFU, 70 to 84

days post-treatment), microbiological cure rate, time to resolution of

symptoms, rate of UTI relapse, rate of adverse events and the pharmacokinetic

profile of fosfomycin.

# Study description

### Background summary

Due to rising resistance of Enterobacteriaceae against the orally available antibiotics ciprofloxacin and trimethoprim-sulfamethoxazole, difficulties arise in the treatment of febrile urinary tract infection (FUTI) in men. Fosfomycin possesses a high bactericidal activity to Escherichia coli with resistance rates of 1%. Fosfomycin 3000mg, dosed every 24 hours, reaches sufficient antibiotic levels in urine, prostate and bladder, has good tolerability and is considered safe. Therefore, fosfomycin is a potential alternative antibiotic option for treatment of FUTI in men.

### Study objective

To determine the efficacy of oral fosfomycin in comparison to the standard of care oral ciprofloxacin, in the treatment of FUTI after initial empirical treatment with intravenous antibiotics.

To describe the pharmokinetic profile of men treated with fosfomycin 3 gram

o.d.

### Study design

An open label multicenter pilot study with historical controls

### Intervention

After an empirical intravenous antibiotic treatment an iv-oral switch to oral fosfomycin 3000mg, every 24 hours, up to 14 days. Patients will be compared to historical controls who were included in a randomized trial with similar inclusion criteria and who were treated with oral ciprofloxacin.
Eligible patients who refuse to be treated with fosfomycin, will be treated with ciprofloxacin. Those patients will be asked to participate in the trial for observational purposes only as they can serve as control patients as well.

### Study burden and risks

Patients will be compared to historical controls who were included in a randomized trial with similar inclusion criteria and who were treated with oral ciprofloxacin.
The burden for participants is considered low as patients are treated and evaluated following current clinical practice guidelines and Good Clinical Practice. This study is considered to be of low-risk for the following reasons; the pathogen causing FUTI has documented susceptibility to fosfomycin; patients are not acutely ill at the moment of randomization as they fulfil the criteria for iv-oral switch (and indeed already had effective intravenous antibiotics) and fosfomycin has a good safety profile. Fosfomycin has been used extensively as single-dose oral therapy; previous studies have indicated that fosfomycin is likely to be suitable for treating FUTI in men with a high bio-availability, reaching sufficient levels in urine, prostate and bladder wall. Clinical cure for FUTI has been described in case series. Furthermore, in case of clinical failure of fosfomcycin the patient can always be treated with the gold standard ciprofloxacin as this is part of the in- and exclusion criteria. Overall the future benefit of this trial, obtaining a new antibiotic option for FUTI in men, outweighs the low risks involved for participants.

## 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. Competent male patient aged 18 years or above
2. One or more symptom(s) suggestive of urinary tract infection (dysuria, frequency or urgency*; perineal or suprapubic pain; costo-vertebral tenderness or flank pain)
3. Fever (ear or rectal temp of 38.2 oC or higher, or axillary temp of 38 oC or higher), or history of feeling feverish with shivering or rigors in the past 24 hours
4. Positive urine nitrate test and/or leucocyturia as depicted by positive leukocyte esterase test or microscopy
5. Hospital admission for presumed FUTI and empirical intravenous antibiotic treatment with b-lactams
6. Positive urine (> 103 CFU/ml) culture and/or blood culture with E. coli susceptible to fosfomycin, ciprofloxacin and the empirical intravenous -lactam treatment
7. Fulfilment of criteria for safe iv to oral switch (hemodynamic stability, ability to consume oral antibiotics, no gastrointestinal problems which affect absorption)

## Exclusion criteria

1. Known allergy to fosfomycin or ciprofloxacin
2. Patients with known polycystic kidney disease
3. Patients on permanent renal replacement therapy (hemodialysis or peritoneal dialysis)
4. Patients with history of kidney transplantation
5. Patients with a permanent urinary catheter
6. Patients with chronic renal failure (eGFR <30 ml/min/1.73m3)
7. Patients with renal abcess or pyonephrosis
8. Patients with chronic bacterial prostatitis (defined as recurrent UTI with the same uropathogen and no other clarifying underlying urological disorder)
9. Patients with any diagnosed metastatic E. coli foci
10. Patients with a double-J or nephrostomy catheter
11. Concomitant systemic antibiotic treatment for another reason than FUTI
12. Residence outside the Netherlands
13. Inability to speak or read Dutch , All participants at the Haga Teaching Hospital are also eligible for the pharmacokinetic part of the study.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 13-01-2021 |
| Enrollment: | 30 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Monuril |
| Generic name: | Fosfomycin |
| Registration: | Yes - NL outside intended use |

## Ethics review

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| Approved WMO Date: | 19-04-2019 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 05-02-2020 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 27-02-2020 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 02-04-2020 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 06-09-2021 |
| Application type: | Amendment |

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|---|---|
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |
| Approved WMO Date: | 06-10-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |
| Approved WMO Date: | 26-02-2024 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |
| Approved WMO Date: | 11-03-2024 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>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 |
| --- | --- |
| EudraCT | EUCTR2017-004963-11-NL |
| CCMO | NL64395.098.18 |