

**In- and exclusion criteria**

Inclusion criteria	Exclusion criteria
Hospitalised	Pregnant or nursing women
Competent women (≥18 years), able to give informed consent	Glomerular filtration rate < 30 ml/min/1,73 m <sup>3</sup> or renal replacement therapy
AF-UTI as presumptive diagnosis and primary reason for hospitalisation*	Concomitant systemic antibacterial treatment #
Adequate intravenous antibiotic therapy for ≥48 - ≤120 hours**	Ascertained or presumptive hypersensitivity to the active compounds and/or any excipient of the products or to any quinole
Candidate for safe iv to oral switch as judged by the attending physician	Participation to any trial with an investigational product involved in the 30 days before the screening visit
Urine (≥10 <sup>4</sup> CFU/ml) OR blood culture obtained within 24 hours before or after admission: <i>Escherichia coli</i> , ciprofloxacin S AND fosfomycin S***	Every other laboratory result, clinical condition, disease or treatment that, in investigator's opinion, make the subject non suitable for the study
	Specific comorbidity or diagnosis##
	Contraindications/interactions for any of the active compounds or medication ###
	Patients with inadequate understanding of the study risks or its requirements or unwilling to plan a follow-up visit

## FORECAST studie

\* Acute Febrile Urinary Tract Infections (AF-UTI) are UTI with at least one of the forthcoming systemic symptoms: fever or low temperature ( $\geq 38.0\text{ C}^\circ$  or  $< 36\text{ C}^\circ$ ), rigors, delirium or hemodynamic instability as a result of sepsis requiring intravenous fluids AND at least one of the following local symptoms: lower abdominal pain, low back pain, flank pain or costo-vertebral angle pain or tenderness on physical examination, any of the following symptoms of UTI (dysuria, urinary urgency, urinary frequency, suprapubic/pelvic discomfort, macroscopic hematuria, new urinary incontinence or worsening of pre-existing incontinence). The local study investigator determines the presumptive diagnosis as the primary reason for hospitalisation with consultation of the attending physician.

\*\* Amoxicillin +/- clavulanic acid / 2nd or 3rd cephalosporin/ aminoglycoside/ carbapenem/ fluoroquinolones/ trimethoprim-sulfamethoxazole OR a combination AND in vitro susceptibility of the causative E.coli to at least one of the used agents

\*\*\* If a participating microbiological laboratory only processes urine cultures  $\geq 10^5$  CFU/ml, only these will be included. If an urine or blood culture results in another non-E.coli bacteria that requires antibiotic treatment, the patient should be excluded.

# If prophylactic antibiotic therapy could not be paused during study therapy, the patient should be excluded

## Renal transplant patients, polycystic kidney disease, neutropenia ( $< 500 /\mu\text{l}$ ), paraplegia, long-term indwelling catheters (placed  $\geq 24$  hours before admission), urostomy, ileal loops, double-J catheter, nephrostomy catheter, suprapubic catheter, suspicion/presence of renal abscess, suspicion of septic metastatic foci/endocarditis

### Concurrent use of Tizanidin, Clozapin or Theophylline. If pausing or conversion of this medicine disadvantages the participant, she will be excluded. Patients with a history of tendon disease/disorder related to quinolone treatment. Patients with known risk factors for prolongation of the QT interval. Glucose-6-phosphate dehydrogenase deficiency