Clinical trial results:
Antibiotic treatment for intermittent bladder catheterisation: A randomised controlled trial of once daily prophylaxis (The AnTIC study)

Summary

EudraCT number	2013-002556-32
Trial protocol	GB
Global end of trial date	23 February 2017

Results information

Result version number	v1 (current)
This version publication date	09 June 2018
First version publication date	09 June 2018

Trial information

Trial identification

Sponsor protocol code	ANTIC:6672

Additional study identifiers

ISRCTN number	ISRCTN67145101
ClinicalTrials.gov id (NCT number)	NCT02145338
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Sponsor organisation address	Freeman Hospital, Newcastle upon Tyne, United Kingdom, NE7 7DN
Public contact	Robert Pickard, Newcastle University, 44 1912137139, robert.pickard@ncl.ac.uk
Scientific contact	Robert Pickard, Newcastle University, 44 1912137139, robert.pickard@ncl.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2017
Global end of trial reached?	Yes
Global end of trial date	23 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research question was to determine whether use of antibiotic prophylaxis over 12 months resulted in a clinically significant (real and worthwhile) reduction in the rate of symptomatic, antibiotic-treated urinary tract infection (UTI) suffered by people performing intermittent self-bladder catheterisation compared to no prophylaxis. We also calculated which treatment strategy gives best value for money to patients and the NHS by measuring the cost per urinary infection avoided by use of antibiotic prophylaxis.

During the first 12 months of the trial we determined whether recruitment to planned trial duration and sample size was going to succeed by monitoring numbers of randomised participants. Specific objectives for the first phase of the study was to find out how quickly individual research sites could begin to recruit patients to the trial, to find out how many eligible patients are identified and how many of those agree to participate per month.

Protection of trial subjects:

The investigational medicinal products (IMP) used in the trial are all licensed in dosage and form for use in prophylaxis against UTI in the UK and are standard care for this indication. From this it was judged that from an IMP perspective the risk to participants was no higher that of standard care.
Any adverse effects associated with the use of antibiotic prophylaxis related to individual agents or changes to normal bacterial flora, were described and minimized by carefully worded trial information given to participants to enable selection of the individually most appropriate agent and information concerning use of oral probiotics.
Participants with symptomatic urinary tract infection were encouraged to also take a catheter specimen of urine (CSU) to their treating clinician for local analysis according to local protocols.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 404
Worldwide total number of subjects	404
EEA total number of subjects	404

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	223
From 65 to 84 years	172
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Recruitment took place between November 2013 and January 2016 through 51 primary and secondary care NHS research sites in England and Scotland. Sites were grouped around six UK hubs in Newcastle upon Tyne, Wakefield, Cambridge, Bristol, Southampton, Aberdeen and Glasgow.

Pre-assignment

Screening details:

Participants were identified when attending secondary care clinics, by search of NHS health records and from commercial organisations providing NHS care. Participants meeting inclusion criteria and willing to participate were consented to take part in the study. Those already taking antibiotic prophylaxis underwent a 3-month washout period.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The study design did not allow blinding of participants, clinicians or local research teams to allocation, although outcome assessors including laboratory staff and members of the central trial team involved in outcome adjudication were blinded to allocated group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Antibiotic Prophylaxis

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Trimethoprim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily Trimethoprim (100mg)

Investigational medicinal product name	Nitrofurantoin
Investigational medicinal product code	
Other name	Aratoin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily Nitrofurantoin 50 mg (or 100 mg dependent on participant weight).

Investigational medicinal product name	Cefalexin
Investigational medicinal product code	
Other name	Ospexin, Tenkorex, Kiflone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once daily Cefalexin 250mg.

Arm title	No Prophylaxis

Arm description: -

Arm type	Standard Care

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Antibiotic Prophylaxis	No Prophylaxis
Started	203	201
Completed	203	201

Period 2	
Period 2 title	Primary analysis point
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Antibiotic Prophylaxis
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Trimethoprim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Once daily Trimethoprim (100mg)	
Investigational medicinal product name	Nitrofurantoin
Investigational medicinal product code	
Other name	Aratoin
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Once daily Nitrofurantoin 50 mg (or 100 mg dependent on participant weight).	
Investigational medicinal product name	Cefalexin
Investigational medicinal product code	
Other name	Ospexin, Tenkorex, Kiflone
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Once daily Cefalexin 250mg.

Arm title	No Prophylaxis
Arm description: -	
Arm type	Standard Care
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Antibiotic Prophylaxis	No Prophylaxis
Started	203	201
Completed	181	180
Not completed	22	21
Consent withdrawn by subject	16	14
Death	-	1
Excluded from analysis insufficient data	6	6

Period 3	
Period 3 title	12 month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Antibiotic Prophylaxis
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Trimethoprim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Once daily Trimethoprim (100mg)	
Investigational medicinal product name	Nitrofurantoin
Investigational medicinal product code	
Other name	Aratoin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Once daily Nitrofurantoin 50 mg (or 100 mg dependent on participant weight).	
Investigational medicinal product name	Cefalexin
Investigational medicinal product code	
Other name	Ospexin, Tenkorex, Kiflone
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Once daily Cefalexin 250mg.	
Arm title	No Prophylaxis
Arm description: -	
Arm type	Standard Care
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Antibiotic Prophylaxis	No Prophylaxis
Started	181	180
Completed	181	180

Baseline characteristics

Reporting groups	
Reporting group title	Antibiotic Prophylaxis
Reporting group description: -	
Reporting group title	No Prophylaxis

Reporting group description: -

Reporting group values	Antibiotic Prophylaxis	No Prophylaxis	Total
Number of subjects	203	201	404
Age categorical Units: Subjects			
Adults (18-64 years)	114	109	223
From 65-84 years	86	86	172
85 years and over	3	6	9
Age continuous Units: years			
arithmetic mean	59.1	60.1	
standard deviation	± 17.0	± 15.6	-
Gender categorical Units: Subjects			
Female	88	87	175
Male	115	114	229
Number of UTI episodes			
Number of UTI episodes suffered in the 12 months prior to randomisation			
Units: Subjects			
<4	71	78	149
>=4	132	123	255
Cause of bladder dysfunction Units: Subjects			
Neurological	80	78	158
Non-neurological	123	123	246
Type of intermittent catheterisation Units: Subjects			
By self	201	198	399
By spouse/carer	1	2	3
Missing	1	1	2
Planned future duration of need for intermittent catheterisation Units: Subjects			
Between 1 and 2 years	0	4	4
Between 2 and 5 years	0	1	1
Indefinite	182	181	363
Not known	20	14	34
Missing	1	1	2
Route of intermittent catheterisation Units: Subjects			
Urethra	196	195	391
Mitrofanoff	6	5	11

Missing	1	1	2
Type of catheter used Units: Subjects			
Single use	200	199	399
Re-useable	2	2	4
Missing	1	0	1
Hydrophillic coated catheter used? Units: Subjects			
No	9	8	17
Yes	189	192	381
Missing	5	1	6
Main functional reason for requiring intermittent catheterisation Units: Subjects			
Bladder outlet obstruction	49	56	105
Bladder failure (underactivity)	139	128	267
Bladder augmentation / replacement	13	16	29
Missing	2	1	3
Central laboratory culture of urine at baseline Units: Subjects			
Negative	93	84	177
Positive	76	77	153
Missing	34	40	74
Creatinine clearance Units: CrCl (mL/min)			
median	89.8	99.1	
inter-quartile range (Q1-Q3)	68.6 to 121.4	71.9 to 124.2	-
Frequency of CISC (/24 hours)			
Frequency of clean intermittent self catheterisation in a 24 hour period.			
Units: Number of times			
arithmetic mean	3.8	4.1	
standard deviation	± 2.2	± 2.9	-
Episodes of UTI in last 12 months			
Episodes of UTI experienced by participant in the last 12 months			
Units: Episodes			
median	4.0	4.0	
inter-quartile range (Q1-Q3)	3.0 to 6.0	3.0 to 7.0	-
Positive urine culture reports in the last 12 months Units: Number			
median	2.0	2.0	
inter-quartile range (Q1-Q3)	1.0 to 4.0	1.0 to 4.0	-
Months use of antibiotic prophylaxis in last 12 months Units: Months			
median	0.0	0.0	
inter-quartile range (Q1-Q3)	0.0 to 1.0	0.0 to 1.0	-

End points

End points reporting groups

Reporting group title	Antibiotic Prophylaxis
Reporting group description: -	
Reporting group title	No Prophylaxis
Reporting group description: -	
Reporting group title	Antibiotic Prophylaxis
Reporting group description: -	
Reporting group title	No Prophylaxis
Reporting group description: -	
Reporting group title	Antibiotic Prophylaxis
Reporting group description: -	
Reporting group title	No Prophylaxis
Reporting group description: -	

Primary: Occurrence of symptomatic antibiotic-treated UTI

End point title	Occurrence of symptomatic antibiotic-treated UTI

End point description:

Occurrence of clinical UTI was defined as the presence of symptoms together with taking a treatment course of antibiotic for UTI. This was measured by participant return of a UTI record for each event, as well as 3-monthly participant questionnaire and 3-monthly trial visit case report form (CRF) completed by the local research team.

End point type	Primary

End point timeframe:

Occurrence of symptomatic antibiotic-treated UTI over 12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	180		
Units: UTI				
All eligible	235	450		

Statistical analyses

Statistical analysis title	Symptomatic antibiotic treated UTI

Statistical analysis description:

Results of performing Poisson regression (incidence rate ratio approach) for primary outcome: number of symptomatic antibiotic-treated UTI.

Comparison groups	Antibiotic Prophylaxis v No Prophylaxis

Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Poisson regression
Parameter estimate	Incidence Rate Ratio
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.04

Primary: Occurrence of symptomatic antibiotic-treated UTI (baseline <4)

End point title	Occurrence of symptomatic antibiotic-treated UTI (baseline <4)
End point description:	
Sub group analysis for participants with Baseline UTI <4	
End point type	Primary
End point timeframe:	
Occurrence of symptomatic antibiotic-treated UTI over 12 months	

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	68		
Units: UTI				
Baseline UTI <4	55	118		

Statistical analyses

Statistical analysis title	Symptomatic antibiotic treated UTI
Comparison groups	Antibiotic Prophylaxis v No Prophylaxis
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Poisson regression
Parameter estimate	Incidence Rate Ratio
Point estimate	0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.64
Variability estimate	Standard error of the mean
Dispersion value	0.08

Primary: Occurence of symptomatic antibiotic treated UTI (baseline >=4)

End point title	Occurence of symptomatic antibiotic treated UTI (baseline >=4)
End point description:	
Sub group analysis for participants with baseline UTI >=4	
End point type	Primary
End point timeframe:	
Occurrence of symptomatic antibiotic-treated UTI over 12 months	

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: UTI				
Baseline episodes of UTI >=4	180	332		

Statistical analyses

Statistical analysis title	symptomatic antibiotic-treated UTI
Comparison groups	Antibiotic Prophylaxis v No Prophylaxis
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Poisson Regression
Parameter estimate	Incidence Rate Ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.64
Variability estimate	Standard error of the mean
Dispersion value	0.05

Primary: Occurrence of symptomatic antiobiotic-treated UTI (adjusted for days at risk)

End point title	Occurrence of symptomatic antiobiotic-treated UTI (adjusted for days at risk)

End point description:

Secondary analysis of primary outcome, adjusted for days at risk

End point type	Primary

End point timeframe:

Occurrence of symptomatic antibiotic-treated UTI over 12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	180		
Units: UTI				
All eligible	235	450		

Statistical analyses

Statistical analysis title	Symptomatic antibiotic-treated UTI

Statistical analysis description:

Adjusted for days at risk

Comparison groups	No Prophylaxis v Antibiotic Prophylaxis
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Poisson Regression
Parameter estimate	Incidence Rate Ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.04

Primary: Occurrence of symptomatic antiobiotic-treated UTI (adjusted for days at risk and stratification)

End point title	Occurrence of symptomatic antiobiotic-treated UTI (adjusted

	for days at risk and stratification)

End point description:

Secondary analysis of primary outcome adjusted for days at risk and stratification factors

End point type	Primary

End point timeframe:

Occurrence of symptomatic antibiotic-treated UTI over 12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	180		
Units: UTI				
All eligible	235	450		

Statistical analyses

Statistical analysis title	Occurrence of symptomatic antiobiotic-treated UTI
Comparison groups	Antibiotic Prophylaxis v No Prophylaxis
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Poisson Regression
Parameter estimate	Incidence Rate Ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.04

Secondary: Treatment Satisfaction (TSQM)

End point title	Treatment Satisfaction (TSQM)

End point description:

Satisfaction with treatment measured using the Treatment Satisfaction with Medication Questionnaire (TSQM). Maximum rating = 100 for each domain.
Using ANCOVA modelling to compare arms (adjusting for stratification factors):
Effectiveness p<0.001
Side-effects p=0.94
Convenience p<0.001
Overall p<0.001
Overall satisfaction score for prophylaxis participants was 74. The TSQM is not validated for 'no treatment' strategies in an open-label RCT setting but overall this group rated mean overall satisfaction as 63.

End point type	Secondary

End point timeframe:
12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144[1]	109[2]		
Units: Scale Score				
arithmetic mean (standard deviation)				
Effectiveness	78.0 (± 19.1)	66.3 (± 19.5)		
Side-effects	67.4 (± 23.4)	67.2 (± 24.2)		
Convenience	88.9 (± 13.9)	78.2 (± 21.4)		
Overall satisfaction	73.8 (± 25.4)	63.0 (± 24.3)		

Notes:
[1] - Effectiveness n=144, Side-effects n=22, Convenience n=144, Overall n=143
[2] - Effectiveness n=108, Side-effects n=32, Convenience n=109, Overall n=109

Statistical analyses

No statistical analyses for this end point

Secondary: eGFR at Baseline and 12 months

End point title	eGFR at Baseline and 12 months

End point description:
Estimated Glomerular Filtration Rate (eGFR) measuring kidney function with comparison between arms

End point type	Secondary

End point timeframe:
Baseline and 12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis	Antibiotic Prophylaxis	No Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200[3]	197[4]	123[5]	140[6]
Units: ml/minute				
arithmetic mean (standard deviation)	86.6 (± 30.2)	88.0 (± 26.1)	82.3 (± 30.0)	83.3 (± 27.6)

Notes:
[3] - Baseline
[4] - Baseline
[5] - 12 months
[6] - 12 months

Statistical analyses

No statistical analyses for this end point

Secondary: Change in eGFR from Baseline

End point title	Change in eGFR from Baseline

End point description:
Change in estimated glomerular filtration rate (eGFR) at 12 months from baseline.

End point type	Secondary

End point timeframe:
12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	138		
Units: ml/minute				
arithmetic mean (standard deviation)	-2.1 (± 15.0)	-3.4 (± 14.2)		

Statistical analyses

Statistical analysis title	Change in eGFR at 12 months
Comparison groups	No Prophylaxis v Antibiotic Prophylaxis
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	ANCOVA

Secondary: ALT at Baseline and 12 months

End point title	ALT at Baseline and 12 months

End point description:
Serum alanine transaminase (ALT) measured at baseline and 12 months, with comparison between arms.

End point type	Secondary

End point timeframe:
Baseline and 12 months

End point values	Antibiotic Prophylaxis	No Prophylaxis	Antibiotic Prophylaxis	No Prophylaxis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	198[7]	188[8]	118[9]	135[10]
Units: U/L				
arithmetic mean (standard deviation)	24.7 (± 19.9)	24.1 (± 15.6)	26.1 (± 19.1)	24.0 (± 14.1)

Notes:

[7] - Baseline

[8] - Baseline

[9] - 12 months
[10] - 12 months

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ALT at 12 months	
End point title	Change in ALT at 12 months
End point description: Change in serum alanine transaminase (ALT) at 12 months	
End point type	Secondary
End point timeframe: 12 months	

End point values	Antibiotic Prophylaxis	No Prophylaxis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	128		
Units: U/L				
arithmetic mean (standard deviation)	1.2 (± 19.5)	-0.3 (± 14.7)		

Statistical analyses

Statistical analysis title	Change in ALT at 12 months
Comparison groups	Antibiotic Prophylaxis v No Prophylaxis
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported for the duration of the trial and for 4 weeks after the trial intervention was stopped.

Assessment type	Systematic

Dictionary used

Dictionary name	Verbatim
Dictionary version	1.0

Reporting groups

Reporting group title	Antibiotic Prophylaxis
Reporting group description: -	
Reporting group title	No Prophylaxis

Reporting group description: -

Serious adverse events	Antibiotic Prophylaxis	No Prophylaxis	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 203 (9.85%)	22 / 201 (10.95%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Bilateral pulmonary embolism			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Polypharmacy	Additional description: Falls and confusion, left sided pneumonia		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Car accident	Additional description: Admitted for medical observation after car accident		

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Admitted to hospital for observation and review	Additional description: CT head - new intracranial changes		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain, dizziness and vomiting			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Collapsed while driving	Additional description: ?CVA, ?seizure disorder		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache and nausea	Additional description: Emergency admission to hospital		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache and right-sided neck pain	Additional description: Shunt malfunction		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical fall			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rigors	Additional description: On parenteral nutrition		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident	Additional description: bilateral femoral fractures and right distal tibial fracture		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizures and collapse			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unable to catheterise Mitrofanoff adequately			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasovagal episode			
subjects affected / exposed	0 / 203 (0.00%)	2 / 201 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Abdominal aortic aneurysm			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma attack	Additional description: Acute asthma attack and anxiety		

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest infection			
subjects affected / exposed	0 / 203 (0.00%)	2 / 201 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Triple bypass surgery			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysphagia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis relapse			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right-sided weakness attributed to somatoform disorder			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transverse myelitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Neuromyelitis optica			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal cancer metastatic			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal pain due to faecal loading			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain/constipation			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epigastric pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal impaction			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforated appendix			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Recurrent vomiting and generalised abdominal discomfort			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Adverse drug reaction	Additional description: Asymptomatic highly raised serum liver enzyme alanine transaminase (ALT)		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder cancer			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematuria post TURP			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria post intravesical botulinum toxin			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trans-urethral resection of bladder tumour			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sub-meatal and urethral strictures			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Follicular thyroid cancer			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fall	Additional description: Fall resulting in fractured spine		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute chronic back pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis	Additional description: Right foot, diagnosed with Charcot's joint.		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post microdiscectomy recurrent lumbar pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ankle stabilisation			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ruptured left quadriceps tendon			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Hickman line infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Percutaneous gastric feeding tube site infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Antibiotic Prophylaxis	No Prophylaxis	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 203 (31.53%)	55 / 201 (27.36%)	
Vascular disorders			
painful varicocele			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Ruptured blood vessel left foot			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
ACE			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Biopsy for microcalcification of lump, left breast			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Biopsy of skin lesion			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Bladder pressure test for neobladder			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Botox treatment			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Corrective surgery to right foot			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Cystoscopy			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective admission for dilatation of mitrofanoff and neo bladder washout			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective admission for SCS insertion			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective admission for stricture dilatation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective day case for embolisation of varicocele			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective microdisectomy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective perineal proctectomy			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective surgery to investigate thickening in bladder wall			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective TURP			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective TURP leading to long term catheterisation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Endoscopy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Fasciectomy (routine planned admission)			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Elective admission for revision of Mitrofanoff			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Knee replacement			
subjects affected / exposed	1 / 203 (0.49%)	1 / 201 (0.50%)	
occurrences (all)	1	1	
Elective mastoidectomy			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Neo vascular surgery (AMD) to right eye			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Botox injection for overactive bladder			
subjects affected / exposed	2 / 203 (0.99%)	0 / 201 (0.00%)	
occurrences (all)	2	0	
Sacral nerve stimulation for overactive bladder			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective thyroid surgery			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Elective below knee amputation			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Rectal irrigation for constipation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Biopsy of prostate			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Transurethral prostatectomy			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Abnormal GGT noted on checking routine liver function			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Achilles			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Admitted to EAU for headache			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Adverse reaction to Nitrofurantoin			
subjects affected / exposed	2 / 203 (0.99%)	0 / 201 (0.00%)	
occurrences (all)	2	0	
Attended AE ?DVT			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Attended AE for ? TIA			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Attended ED with ? chest pain. Discharged same night			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Attended ED with increase swollen leg, woozy and light-headed	Additional description: possible side effect of Citalopram		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Attended ED for ? obstructed bowel. Discharged same day			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Migraine (issue with shunt?)			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Attended A&E for ? cause			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Blackout whilst driving			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Car accident	Additional description: car reversed into patient		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Cat bite			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Collapse of right leg			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Lower back pain and groin pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Contusion (head)			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Decline in WCC			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Generalised joint pain of sudden onset			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Head cold			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Hoarseness (exacerbation)			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
pain right wrist			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
pain and discomfort in toes of both feet			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Reaction to Nitrofurantoin prescribed for UTI			
subjects affected / exposed	1 / 203 (0.49%)	1 / 201 (0.50%)	
occurrences (all)	1	1	
Elevated potassium			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Vulval lumps	Additional description: Antibiotic given for ? infection		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Thinning hair			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Blotchy rash on back			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Rash on inner arms, palms and back of neck			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Patient reported collapse on the way to buy papers			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Pulled VP shunt			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Pressure sore			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	2	
Pruritis vulvae			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
PV bleed			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Reaction to flucloxacillin			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Reaction to trimethoprim			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Scalp itchiness			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Sore throat			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Stomach discomfort			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Stopped prophylactic cephalexin due to stomach issues			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Stopped prophylactic antiobiotics on microbiologist advice			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Weight loss			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Breathless			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Chest infection			
subjects affected / exposed	0 / 203 (0.00%)	2 / 201 (1.00%)	
occurrences (all)	0	2	
Chesty cough			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Common cold			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Cough (exacerbation)			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Bronchiectasis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	3 / 203 (1.48%)	3 / 201 (1.49%)	
occurrences (all)	3	3	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Investigations			
Ultrasound investigation	Additional description: Found hydrocele in right testicle and bilateral epydidimal cysts		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Routine cystoscopy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Urodynamics			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Burn right foot, infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Fall due to back pain after sneezing			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Fractured ribs due to fall			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Injury to urethra from catheter			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Post op redness of second toe			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Severe pain right knee due to fall			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 203 (0.49%)	1 / 201 (0.50%)	
occurrences (all)	1	1	
Night sweats increased			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Epileptic fit			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Decline in WBC and platelets	Additional description: Study drug discontinued		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Increased tinnitus following VP shunt revision			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Anteria Uveitis left eye			

subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Fluid behind eyes bilaterally			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Blurred vision			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Diarrhoea and sickness			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 203 (0.49%)	1 / 201 (0.50%)	
occurrences (all)	1	4	
Diarrhoea and vomiting			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Mild intermittent nausea			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	4	0	
Nausea			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Pancreatitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Viral gastroenteritis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	

Skin and subcutaneous tissue disorders			
Two actinic keratoses on left side of upper nose			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Rash on chest, legs and feet			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Basal cell carcinoma	Additional description: Removed with complete excision		
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Blotchy rash			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Exacerbation of dermatitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Exacerbation of leg ulcers			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	2	
Itchy rash			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Itchy skin with excoriation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Admitted to Emergency assessment unit for query renal colic			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Attended ED for UTO			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Decline in renal function noted in	Additional description: Prophylaxis stopped		

biochemistry			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Frank haematuria caused by kink in hi catheter			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Frank haematuria requiring flexible cystoscopy			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Frank haematuria with pre-existing non functioning right kidney			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Haematuria and retention			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Left renal cyst increase in size to 5cm			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Pain in transplanted kidney			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Nocturia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Incontinence			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Frank blood in urine			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Periodic urethritis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Renal pain			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Thickening of bladder wall			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Acupuncture for back pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Back pain/fall			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Cervical spondylosis (exacerbation)			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Tennis elbow, cortisone injection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Decompression of L4 and L5 through degenerative changes			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Pain base of right thumb	Additional description: exacerbation osteoarthritis		
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Infections and infestations			
Dental abscess			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	2	
Oral infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Oral thrush and constipation			

subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Thrush in mouth			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Yeast infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Septic toe			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Sinus infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Slight infection to left teste			
subjects affected / exposed	0 / 203 (0.00%)	1 / 201 (0.50%)	
occurrences (all)	0	1	
Tennis elbow, infected soft tissue			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Thrush			
subjects affected / exposed	2 / 203 (0.99%)	1 / 201 (0.50%)	
occurrences (all)	2	1	
Tonsillitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	
Wound infection to knee after fall			
subjects affected / exposed	1 / 203 (0.49%)	0 / 201 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2013	Widening of inclusion criteria to include those who had had one serious UTI – in line with options that would be offered in standard care. More frequent participant contact – to help participants as much as possible to complete UTI log and avoid ascertainment bias. Payment of any prescription charge to avoid participants being out of pocket. £20 gift to participants on study entry Use of calculated creatinine clearance rather than eGFR – in line with recent NHS guidance for use of nitrofurantoin as UTI prophylaxis.
13 May 2014	The protocol was updated to make it clear that washout participants should be consented at the beginning of the washout period, but not randomised until the washout period was complete The protocol was also amended to clarify that an active, symptomatic UTI did not exclude a participant from the study and that consent to participate could still be taken, but that the UTI should be treated before a participant could be randomised.
14 May 2014	Update to the contraindications section of the SmPC for Nitrofurantoin concerning patients with kidney dysfunction with an eGFR of less than 45 ml/minute. The study protocol and all study documentation were amended to reflect this update.
30 July 2015	Change to the protocol to allow sites to send a second invitation letter to participants who had not responded to the initial invitation to the study.
17 August 2016	Update to clarify the wording around the approved RSI for the study. The RSI contained in section 4.8 of the SmPC for the three antibiotics used in the study was submitted to MHRA for approval. The updated SmPC for nitrofurantoin, trimethoprim and cefalexin were included in the appendices of the new protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29766842