

DRUG UPDATE

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ANTIBIOTIC PROPHYLAXIS FOR RECURRENT UTI IN WOMEN.

Women who have had three or more UTIs in the last 12 months may be considered for continuous UTI antibiotic prophylaxis. There is no good evidence of any differences in efficacy between continuous prophylactic regimens. Trimethoprim should generally be used first: cefalexin and nitrofurantoin may also be considered. Quinolones should be reserved as second line therapy because of their greater expense and concerns regarding the promotion of resistance.

What are the available drug treatments?

Up to 50% of women will suffer from a symptomatic urinary tract infection (UTI) during their lifetime.¹ Up to 20% of non-pregnant women who have cystitis will experience a recurrence. Of these 90% are due to re-infection and about 10% to relapse.² The most common infecting organism is *Escherichia coli*, which is responsible for 70% or more of uncomplicated urinary tract infections in general practice. Others include *Proteus mirabilis*, *Enterococcus faecalis* *Klebsiella pneumoniae* and *Staphylococcus saprophyticus*.^{3,4} Recurrent infection may be due to a re-infection (after successful eradication of infection) or a relapse after inadequate treatment.³ Risk factors for cystitis include prior infection, sexual intercourse and exposure to vaginal spermicide.⁵

Trimethoprim 100 mg nocte, nitrofurantoin 50-100 mg nocte, and cefalexin 125 mg nocte have been recommended for long term UTI prophylaxis.⁴ Norfloxacin 400 mg twice daily is licensed for chronic relapsing UTI for a maximum of 12 weeks.⁴ This document summarises the place in therapy of prophylactic antibiotics to treat recurrent lower UTI in non pregnant women.

How effective are they?

Continuous antibiotic prophylaxis

Several six and twelve month RCTs have been carried out in patients that have had at least two UTIs in the previous 12 months and the primary endpoint was bacterial UTI. One of the two 6 month studies (n = 60) compared cotrimoxazole, trimethoprim, nitrofurantoin and placebo.⁶ The mean number of infections per patient year were 0.15, 0, 0.14 and 2.80 respectively (p<0.001 for placebo vs each active drug treatment). The second compared norfloxacin and nitrofurantoin (n = 94). Infections per patient year were 0.04 and 0.60 respectively (p = 0.05).⁷ The first 12 month RCT compared trimethoprim and nitrofurantoin (n = 72). Infections per patient year were 1.00 and 0.17 respectively (p<0.05).⁸ The second

evaluated norfloxacin vs nitrofurantoin (n = 88); infections per patient year were 0.002 and 0.003 respectively (no p value available).⁹ In a 12 month RCT comparing cefaclor and nitrofurantoin (n = 97), the number of infections per patient year was 0.006 for both drugs.¹⁰

Postcoital prophylaxis

One larger (n= 135) RCT compared ciprofloxacin 125 mg taken daily at night (n = 65) vs ciprofloxacin 125 mg postcoital (n = 70) for 12 months.¹¹ UTI frequency per patient year prior to treatment ranged from 3.62 to 3.66. After treatment this figure was reduced to 0.031 and 0.043 for daily ciprofloxacin and postcoital ciprofloxacin respectively (p<0.0001).

How safe are they?

The most common adverse effects for all agents were gastrointestinal symptoms, rash and candida vaginitis.¹² Adverse events in prophylaxis clinical trials occurred in 7-40% of patients for trimethoprim, 0-40% for nitrofurantoin, 5% for cefaclor, 7-21% for norfloxacin and 13% for ciprofloxacin.¹²

When should treatment be initiated and for how long?

Opinion varies on when a prophylactic antibiotic for a UTI should be started. Prophylaxis can be considered in women who have three or more such infections over a 12 month period.^{5,13,14} Prophylaxis should not be initiated until eradication of active infection is confirmed by a negative culture at least one to two weeks after treatment is discontinued.⁵ After confirmation of a negative urine culture prophylaxis is usually initiated for a trial period of 6 months but has been safely and effectively continued for 2-5 years without the emergence of resistant organisms.⁵ Infections occurring whilst the patient is taking prophylaxis are likely to be resistant to the agent being taken. Treatment of any acute relapse of UTI should

therefore consist of an appropriate alternative drug. Urine culture should be carried out to ensure treatment is with a drug to which the organism is sensitive.¹

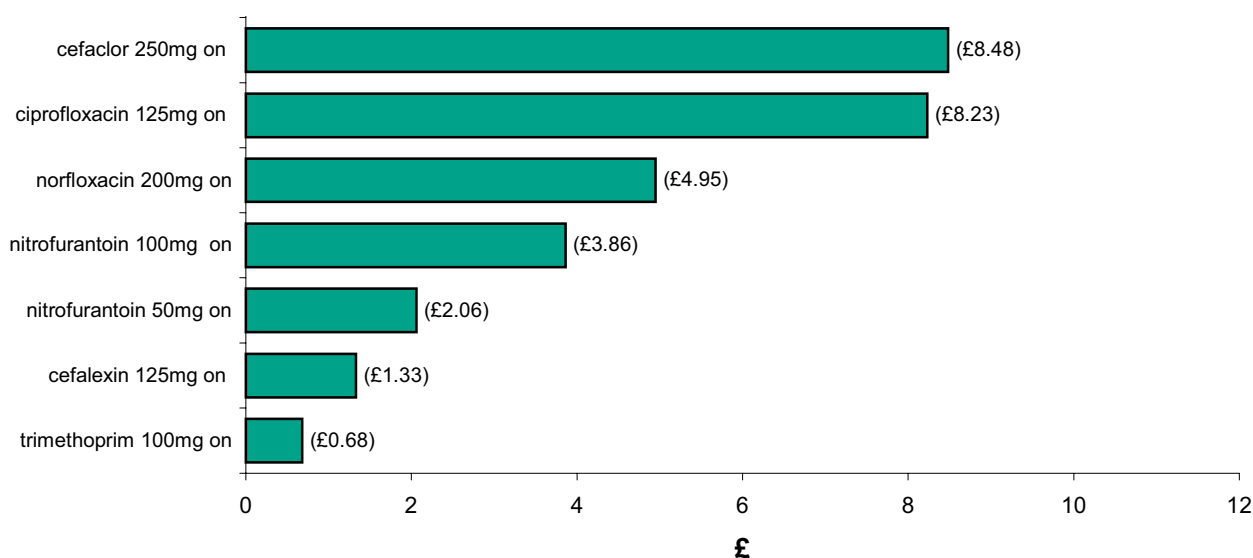
Which antibiotic should be used?

Trimethoprim is still regarded as an effective first choice treatment for uncomplicated UTIs.² There is no consistent difference in recurrence rates

among different continuous prophylactic regimens. Current recommendations from the Health Protection Agency and the BNF suggest trimethoprim, nitrofurantoin and cefalexin should be used first line.^{4,13} Resistance rates to quinolones are less than 5% but the quinolones are generally not regarded as first line therapy because of their greater expense and concerns regarding the promotion of quinolone resistance.¹⁴

How much does it cost?

Cost for 28 days treatment (prices form MIMS/Drug Tariff April 2004)



N.B. Doses shown represent those used in the clinical trials discussed. They are for general comparison only and do not imply therapeutic equivalence

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KEY RCT - randomised controlled trial, CT-controlled trial, G-guidelines, O-open study, MA-meta analysis, R-review, U-unpublished, Abs- abstract, E-editorial

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