

NEW DRUG EVALUATION

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FESOTERODINE

Fesoterodine, a urinary antispasmodic, is licensed for the treatment of symptoms associated with overactive bladder syndrome such as urinary frequency, urgency and incontinence. NICE recommends non-proprietary immediate release oxybutynin as first line drug treatment following non-pharmacological interventions such as pelvic floor muscle exercises and bladder training. Fesoterodine cannot be recommended for prescribing until it is proven to be as effective as, or to have advantages over, the other antimuscarinics that were reviewed by NICE.

What is it?

Fesoterodine (Toviaz[®], Pfizer) is a urinary antispasmodic, in a modified release (MR) preparation, licensed for the treatment of symptoms that may occur in patients with overactive bladder syndrome (OAB); urinary frequency and urinary urgency incontinence (UUI).¹ Fesoterodine is a pro-drug, which after oral administration, is hydrolysed to the same active metabolite as tolterodine.² The starting dose is 4 mg once daily and the dose may be titrated up to 8 mg daily. Full treatment effects are observed 2 - 8 weeks after introduction and re-evaluation of efficacy is recommended after 8 weeks of treatment.¹

How effective is it?

No adequately-powered phase III studies comparing the effectiveness of fesoterodine with other licensed therapies have been published. Only two phase III, randomised, double blind, placebo controlled, multicentre trials have been identified.^{3,4}

In the first study 836 patients were randomised to placebo (n = 274), 4 mg (n = 283) or 8 mg (n = 279) of fesoterodine MR once daily for 12 weeks.³ The primary end point was the change from baseline in the number of micturations per 24 hours.³ Co-primary end points were the change from baseline in the mean number of UUI episodes per 24 hours and the treatment response. Results are summarised below.³

	Micturations / 24 hours	UUI episodes / 24 hr	'% Yes' treatment response
Placebo	-6.9 %	-40.0 %	45 %
4 mg Fesoterodine	-14.9 % (p < 0.001)	-67.4 % (p < 0.001)	64 % (p < 0.001)
8 mg Fesoterodine	-16.0 % (p < 0.001)	-81.8 % (p < 0.001)	74 % (p < 0.001)

'% Yes' to treatment response = % of patients who reported their symptoms had 'greatly improved' or 'improved'

In the second study, patients were randomised to placebo (n = 285), fesoterodine MR 4 mg (n = 272), or 8 mg (n = 288) or tolterodine MR 4 mg (n = 290) for 12 weeks.⁴ The primary and co-primary end points were the same as in the previous study. The results (n = 1103) are summarised below.⁴

	Micturations / 24 hours	UUI episodes / 24 hr	'% Yes' treatment response
Placebo	-11.1 %	-50.0 %	53 %
4 mg Fesoterodine	-16.7 % (p < 0.001)	-80 % (p = 0.001)	75 % (p < 0.001)
8 mg Fesoterodine	-18.6 % (p < 0.001)	-87.5 % (p < 0.001)	79 % (p < 0.001)
4 mg Tolterodine MR	-13.8 % (p = 0.005)	-70.0 % (p = 0.105)	72 % (p < 0.001)

'% Yes' to treatment response = % of patients who reported their symptoms had 'greatly improved' or 'improved'

Both studies had limitations. The drop out rates were high at 19% and 13% respectively.^{3,4} The second study was not powered to detect a statistical difference between fesoterodine and tolterodine MR.^{2,5} Results and conclusions from post hoc analysis should be interpreted cautiously, and are not included in this evaluation.

Patients recorded events in their diaries over 3-day periods. This is not in line with EMEA recommendations, which is that diaries be recorded over a week.²

How safe is it?

As with other antimuscarinic drugs, the most frequent adverse effect was dry mouth, which was more common at the higher dose.^{3,4} Other reported adverse effects were constipation,⁴ headache^{3,4} and urinary tract infection.³ The incidence of urinary retention was not significantly different from placebo.²

All suspected adverse reactions to black triangle drugs such as fesoterodine MR should be reported to the MHRA via the Yellow Card Scheme (www.yellowcard.gov.uk).

What other options are there?

NICE guidance for the management of urinary incontinence in women recommends supervised pelvic floor muscle training for at least 3 months as first line treatment for women with stress or mixed urinary incontinence.⁶ Immediate release non-proprietary oxybutynin should be offered to women as first line drug treatment if bladder training is ineffective as this is the most cost effective option.⁶ If not tolerated, darifenacin, solifenacin, tolterodine,

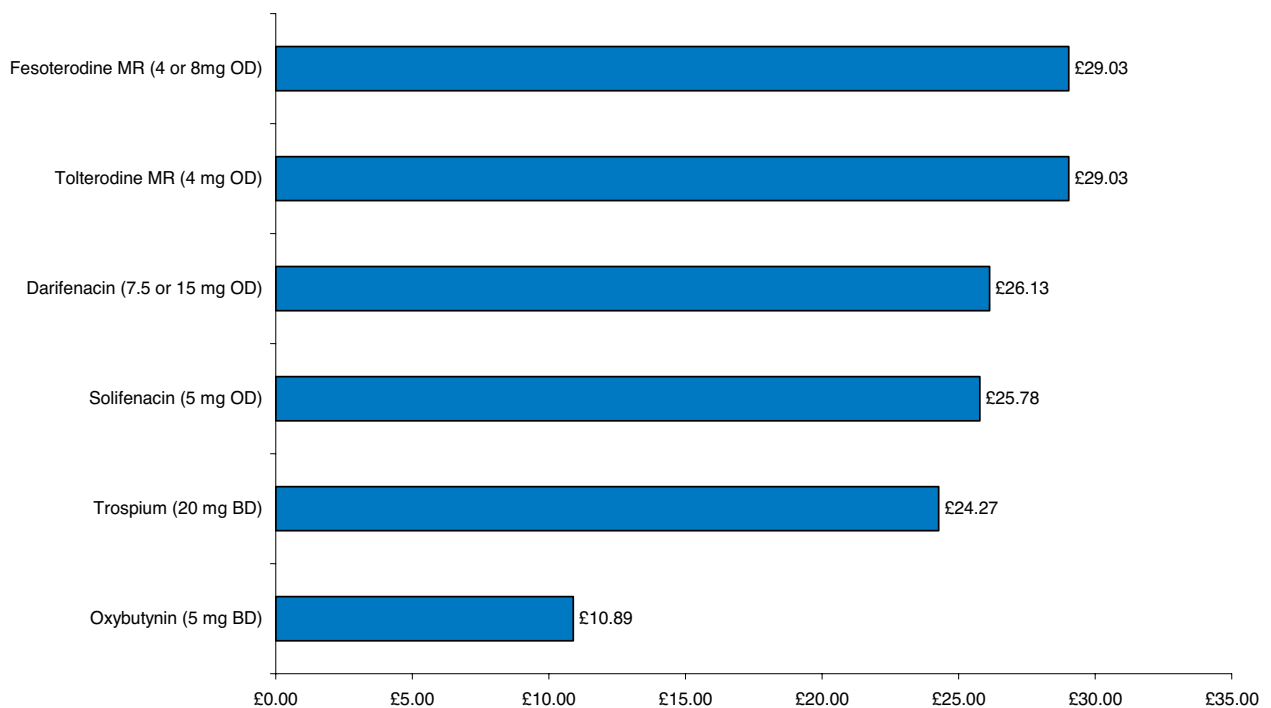
How much does it cost?

trospium, transdermal or MR oxybutynin may be considered. There is no evidence of a clinically important difference in efficacy between antimuscarinic drugs.⁶

When should it be used?

Fesoterodine is not recommended for prescribing as it has not been shown to be as or more effective than the other antimuscarinic agents. Currently it has only been shown to be more effective than placebo. There is no evidence that patients who have failed to respond to, or can not tolerate immediate release oxybutynin, will benefit from fesoterodine.

Cost for 28 days treatment (Source: Drug Tariff & NHS dm&d, July 2008)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence

REFERENCES

1. Pfizer Limited. Summary of Product Characteristics for Toviaz®. www.medicines.org.uk. Updated 17/06/08
2. Scottish Medicines Consortium assessment. Fesoterodine fumarate 4mg and 8mg prolonged release tablets. No. (480/08) 06.06.08.
3. <http://www.scottishmedicines.org.uk/smc/5833.html>
4. Nitti V W et al. Efficacy, safety and tolerability of Fesoterodine for overactive bladder syndrome. The Journal of Urology 2007; 178: 2488-2494 (RCT)
5. Chapple C et al. Clinical efficacy, safety and tolerability of once daily fesoterodine in subjects with overactive bladder. Eur Urology 2007; 52: 1204-1212 (RCT)
6. Chapple C et al. Comparison of fesoterodine and tolterodine in patients with overactive bladder. BJU International; [In press] (R)
7. NICE. Clinical Guideline 40. Urinary incontinence: The management of urinary incontinence in women. London, Oct 2006. (G) <http://www.nice.org.uk>

KEY RCT - randomised controlled trial, R - Review, G - guideline

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