

NEW DRUG EVALUATION

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SOLIFENACIN

Solifenacin is a urinary antispasmodic agent licensed for the treatment of incontinence and increased urinary frequency and urgency. In clinical trials solifenacin produced a modest improvement in the symptoms of overactive bladder. The most common reported adverse reaction was dry mouth. There are no published clinical trials comparing it to oxybutynin, which has a greater evidence base and remains the treatment of choice for patients with an unstable bladder.

What is it?

Solifenacin (Vesicare®, Yamanouchi Pharma) is a urinary antispasmodic agent licensed for the treatment of urge incontinence and/or increased urinary frequency and urgency, as may occur in patients with overactive bladder syndrome.¹ The recommended dose is 5 mg once daily, which may be increased to 10 mg once daily if needed.¹

How effective is it?

Four 12 week randomised, multi-centre, double-blind, placebo controlled studies have been completed and two have been published in full.^{2,3} In the first study 1081 patients were randomised to receive either solifenacin 5 mg or 10 mg once daily, tolterodine 2 mg twice daily or placebo for 12 weeks.² The mean number of urgency episodes/24h at baseline was 5.30 for placebo, 5.77 for solifenacin 5mg, 5.82 for solifenacin 10 mg and 5.45 for tolterodine. Compared with placebo the change from baseline (-1.41, -33%) in the mean number of urgency episodes per 24 hour was lower with solifenacin 5 mg (-2.85, -52%) and 10 mg (-3.07, -55% both $p < 0.001$), but not with tolterodine (-2.05, -38%; $p = 0.0511$). This study did not demonstrate that solifenacin is clinically superior to tolterodine.

In the second study 857 patients were randomised to receive placebo, solifenacin 5 mg or 10 mg once daily.³ The primary objective was the mean number of micturitions/24h. They ranged from 12.05 to 12.31 at baseline and were similar across treatment groups. Compared with changes obtained with placebo (-1.59), micturitions /24h were decreased with solifenacin 5mg (-2.37, $p = 0.0018$) and solifenacin 10 mg (-2.81, $p = 0.0001$).

The results from the four RCT have been pooled together and are available as an abstract.⁴ Although the number of urgency episodes/24 h at baseline and endpoint are not available, the treatment effect (active-placebo differences) were -1.12 and -1.48 episodes for the 5 mg and 10 mg solifenacin respectively. Both of these reductions were statistically significant. The treatment effect for tolterodine 2 mg bd was smaller (-0.64) and was also significant ($p = 0.031$).

How safe is it?

The frequency of anticholinergic adverse reactions are dose related.¹ In one efficacy study ($n = 1081$), although not powered to show a difference when compared to tolterodine 2 mg bd, the incidence of dry mouth was similar to solifenacin 5 mg and 10 mg (19%, 14% and 21% respectively) but constipation (3%, 7% and 8%) and blurred vision (2%, 4% and 6%) occurred more frequently with solifenacin.² Patients discontinuing treatment due to adverse events was 3.7% in the placebo group, 3.2% with solifenacin 5 mg, 2.6% with solifenacin 10mg and 1.9% with tolterodine.²

Similar results were seen in a 40-week open label, long term extension study ($n = 1,633$), where 4.7% patients discontinued open label solifenacin due to adverse effects.⁵ There are no clinical trials comparing solifenacin with oxybutynin.

What other options are there?

Oxybutynin is an established and effective first-line drug for the treatment of patients with an unstable bladder.⁶ However its use is often limited by adverse effects. The most appropriate second-line

drug remains unclear. There are no proven clinical differences between them, and therefore cost, tolerability and convenience will be the main considerations when making a formulary or prescribing decision.

The manufacturer anticipates that solifenacin will be prescribed as an alternative to tolterodine.⁷ Between July 2003 and June 2004, in the former Northern and Yorkshire Region £7 million was spent on tolterodine 2 and 4 mg. 108,018

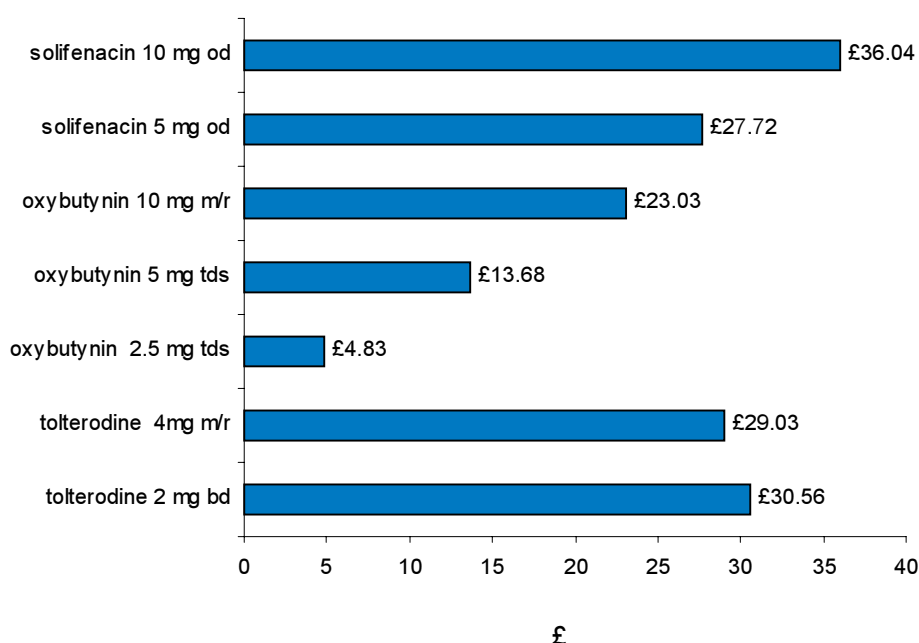
prescriptions were written for tolterodine 2 mg and 123,566 for tolterodine 4mg.

When should it be used?

There are no published clinical trials comparing solifenacin to oxybutynin and it does not appear to offer any significant clinical or tolerance advantages over tolterodine. The role of solifenacin in the treatment of overactive bladder is unclear and until further information becomes available there is no reason to prescribe it.

How much does it cost?

Cost for 28 days treatment (prices from MIMS/Drug Tariff December 2004)



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

REFERENCES

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

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