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Title: LONG-TERM (12 MONTHS) EFFICACY AND TOLERABILITY OF TOLTERODINE ONCE-DAILY IN THE TREATMENT OF OVERACTIVE BLADDER

Aims of study:

Numerous studies have established that the antimuscarinic agent tolterodine, at a dosage of 2mg twice daily, is effective and well tolerated in the treatment of overactive bladder [1–3] and provides effective alleviation of symptoms during long-term therapy [4]. Recently, a new extended-release (ER) capsule formulation of tolterodine has been developed for once-daily treatment of this prevalent and chronic condition. Compared with the existing twice-daily (immediate-release [IR]) tablet formulation, tolterodine ER 4mg once daily demonstrates improved efficacy for reducing urge incontinence episodes and a significantly lower frequency of dry mouth [5]. The aim of the present study was to confirm the long-term efficacy and tolerability of tolterodine ER during a 12-month, open-label extension of treatment.

Methods:

Patients with overactive bladder completing a 12-week, multicentre, double-blind, randomized, parallel-group study with tolterodine IR (2mg twice daily), tolterodine ER (4mg once daily) or placebo were allowed to continue on long-term, open-label treatment with tolterodine ER 4mg once daily for a further 12 months. Efficacy (micturition diary variables) and tolerability (adverse events, withdrawals) and safety were determined throughout long-term treatment.

Results:

From a population of 1337 patients who completed double-blind treatment, 1077 (81%) elected to continue treatment with tolterodine ER (having previously received either placebo [n=339, 32%], tolterodine IR [n=368, 34%] or tolterodine ER [n=370, 34%]). Most patients were female (82%), and a total of 591 (55%) had previously received treatment for overactive bladder. Of these 591, 231 (39%) had a poor efficacy response to other treatment. Overall, the efficacy of tolterodine ER was maintained during long-term treatment, with no evidence for the development of tolerance. Change from baseline in micturition diary variables after 12 months' treatment are shown in the Table. Relative to baseline, the median change in incontinence episodes after 12 months' treatment was –83% ($p<0.0001$).

Change from baseline in micturition diary variables after 12 months' treatment

Variable	Mean change (SD)	P value
Urge incontinence episodes/week	–12.5 (20)	<0.0001
Micturitions/24 hours	–2.3 (3.4)	<0.0001
Pads used/24 hours	–1.4 (2.1)	<0.0001
Volume voided/micturition	43 (60)	<0.0001

Tolterodine ER was well tolerated during long-term treatment, and satisfactory compliance was observed for

>85% of patients. Of the 1075 enrolled patients eligible for safety analysis, 759 (71%) completed 12 months' treatment. The main reasons for discontinuation were adverse events and lack of efficacy (10% each). Dry mouth was the most common adverse event (13% of patients), but rarely troublesome to patients in terms of severity (mild, 7.5%; moderate, 4.2%; severe, 1.2%) or need for treatment discontinuation. Other adverse events occurred in <5% of patients. The overall safety profile of tolterodine ER was excellent, with no clinical relevant changes in laboratory safety parameters. Acute urinary retention was noted for only 2 patients (0.2%).

Conclusions:

Tolterodine ER 4mg once daily is a convenient, well tolerated antimuscarinic therapy that maintains efficacy over time in patients with overactive bladder.

References

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Supported by Pharmacia Corporation.