# *Supplementary data:* Cost-effectiveness of mirabegron compared to tolterodine ER 4 mg for overactive bladder in Canada

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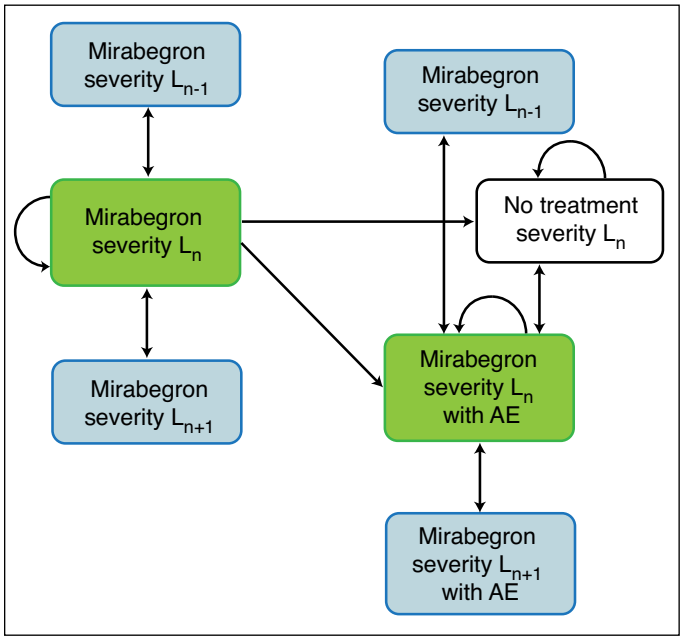


***Supplementary Fig. 1.*** Possible health state transitions in the model. Ln-1 indicates a lower level of OAB symptom severity, Ln+1 a higher level of severity, and Ln the same level of severity. AE: adverse event; OAB: overactive bladder.

**Supplementary Table 1. Transition matrices for frequency of micturition and incontinence episodes**

**A. Micturition, baseline to 1 month, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 1 month | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at baseline | 1 | 0.825 | 0.163 | 0.010 | 0.002 | 0.000 |
| | 2 | 0.442 | 0.446 | 0.100 | 0.011 | 0.002 |
| | 3 | 0.184 | 0.392 | 0.321 | 0.078 | 0.025 |
| | 4 | 0.066 | 0.213 | 0.358 | 0.240 | 0.123 |
| | 5 | 0.036 | 0.078 | 0.152 | 0.233 | 0.501 |

**B. Micturition, 1–2 months, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 2 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 1 month | 1 | 0.784 | 0.194 | 0.018 | 0.004 | 0.001 |
| | 2 | 0.367 | 0.463 | 0.145 | 0.021 | 0.004 |
| | 3 | 0.125 | 0.332 | 0.380 | 0.124 | 0.039 |
| | 4 | 0.036 | 0.147 | 0.346 | 0.313 | 0.158 |
| | 5 | 0.017 | 0.046 | 0.126 | 0.259 | 0.551 |

**C. Micturition, 2–3 months and subsequent months, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 3 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 2 months | 1 | 0.759 | 0.216 | 0.020 | 0.003 | 0.001 |
| | 2 | 0.334 | 0.485 | 0.158 | 0.019 | 0.004 |
| | 3 | 0.110 | 0.337 | 0.400 | 0.108 | 0.045 |
| | 4 | 0.032 | 0.149 | 0.365 | 0.273 | 0.181 |
| | 5 | 0.014 | 0.045 | 0.127 | 0.216 | 0.599 |

**D. Micturition, baseline–1 month, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 1 month | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at baseline | 1 | 0.795 | 0.188 | 0.013 | 0.003 | 0.000 |
| | 2 | 0.391 | 0.474 | 0.117 | 0.015 | 0.002 |
| | 3 | 0.148 | 0.378 | 0.342 | 0.103 | 0.029 |
| | 4 | 0.048 | 0.186 | 0.347 | 0.290 | 0.128 |
| | 5 | 0.025 | 0.066 | 0.141 | 0.270 | 0.498 |

**E. Micturition, 1–2 months, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 2 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 1 month | 1 | 0.749 | 0.222 | 0.022 | 0.006 | 0.001 |
| | 2 | 0.318 | 0.481 | 0.167 | 0.030 | 0.005 |
| | 3 | 0.097 | 0.309 | 0.392 | 0.159 | 0.043 |
| | 4 | 0.026 | 0.124 | 0.325 | 0.366 | 0.159 |
| | 5 | 0.012 | 0.038 | 0.115 | 0.296 | 0.539 |

**Supplementary Table 1 (cont'd). Transition matrices for frequency of micturition and incontinence episodes**

**F. Micturition, 2–3 months and subsequent months, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 3 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 2 months | 1 | 0.722 | 0.246 | 0.026 | 0.005 | 0.001 |
| | 2 | 0.287 | 0.501 | 0.180 | 0.026 | 0.005 |
| | 3 | 0.085 | 0.314 | 0.412 | 0.139 | 0.050 |
| | 4 | 0.023 | 0.128 | 0.345 | 0.322 | 0.183 |
| | 5 | 0.004 | 0.021 | 0.092 | 0.264 | 0.619 |

**G. Micturition, no treatment**

| No treatment | | Severity level at (n+1) months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at n months | 1 | 0.063 | 0.296 | 0.262 | 0.187 | 0.193 |
| | 2 | 0.063 | 0.296 | 0.262 | 0.187 | 0.193 |
| | 3 | 0.063 | 0.296 | 0.262 | 0.187 | 0.193 |
| | 4 | 0.063 | 0.296 | 0.262 | 0.187 | 0.193 |
| | 5 | 0.063 | 0.296 | 0.262 | 0.187 | 0.193 |

**H. Incontinence, baseline–1 month, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 1 month | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at baseline | 1 | 0.838 | 0.136 | 0.014 | 0.005 | 0.006 |
| | 2 | 0.420 | 0.444 | 0.085 | 0.032 | 0.018 |
| | 3 | 0.302 | 0.393 | 0.158 | 0.104 | 0.043 |
| | 4 | 0.133 | 0.315 | 0.187 | 0.213 | 0.151 |
| | 5 | 0.077 | 0.119 | 0.149 | 0.152 | 0.503 |

**I. Incontinence, 1–2 months, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 2 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 1 month | 1 | 0.843 | 0.124 | 0.018 | 0.006 | 0.009 |
| | 2 | 0.422 | 0.404 | 0.109 | 0.039 | 0.025 |
| | 3 | 0.290 | 0.341 | 0.193 | 0.120 | 0.056 |
| | 4 | 0.119 | 0.255 | 0.212 | 0.229 | 0.186 |
| | 5 | 0.062 | 0.086 | 0.152 | 0.146 | 0.555 |

**J. Incontinence, 2 to 3 months and subsequent months, mirabegron 50 mg**

| Mirabegron 50 mg | | Severity level at 3 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 2 months | 1 | 0.807 | 0.158 | 0.018 | 0.007 | 0.010 |
| | 2 | 0.368 | 0.469 | 0.096 | 0.039 | 0.027 |
| | 3 | 0.253 | 0.397 | 0.170 | 0.121 | 0.059 |
| | 4 | 0.102 | 0.293 | 0.185 | 0.227 | 0.193 |
| | 5 | 0.053 | 0.098 | 0.132 | 0.144 | 0.574 |

**Supplementary Table 1 (cont'd). Transition matrices for frequency of micturition and incontinence episodes**

**K. Incontinence, baseline–1 month, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 1 month | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at baseline | 1 | 0.852 | 0.120 | 0.015 | 0.005 | 0.008 |
| | 2 | 0.443 | 0.408 | 0.093 | 0.032 | 0.024 |
| | 3 | 0.315 | 0.357 | 0.170 | 0.102 | 0.055 |
| | 4 | 0.135 | 0.278 | 0.195 | 0.203 | 0.190 |
| | 5 | 0.070 | 0.094 | 0.140 | 0.129 | 0.567 |

**L. Incontinence, 1–2 months, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 2 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 1 month | 1 | 0.855 | 0.109 | 0.019 | 0.006 | 0.011 |
| | 2 | 0.442 | 0.368 | 0.118 | 0.038 | 0.033 |
| | 3 | 0.299 | 0.307 | 0.205 | 0.117 | 0.072 |
| | 4 | 0.118 | 0.220 | 0.218 | 0.214 | 0.230 |
| | 5 | 0.055 | 0.067 | 0.140 | 0.122 | 0.616 |

**M. Incontinence, 2–3 months and subsequent months, tolterodine ER 4 mg**

| Tolterodine ER 4 mg | | Severity level at 3 months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at 2 months | 1 | 0.822 | 0.140 | 0.019 | 0.007 | 0.013 |
| | 2 | 0.389 | 0.432 | 0.105 | 0.039 | 0.035 |
| | 3 | 0.263 | 0.360 | 0.183 | 0.118 | 0.077 |
| | 4 | 0.102 | 0.254 | 0.191 | 0.213 | 0.240 |
| | 5 | 0.036 | 0.053 | 0.120 | 0.112 | 0.679 |

**N. Incontinence, no treatment**

| No treatment | | Severity level at (n+1) months | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 |
| Severity level at n months | 1 | 0.299 | 0.187 | 0.163 | 0.105 | 0.247 |
| | 2 | 0.299 | 0.187 | 0.163 | 0.105 | 0.247 |
| | 3 | 0.299 | 0.187 | 0.163 | 0.105 | 0.247 |
| | 4 | 0.299 | 0.187 | 0.163 | 0.105 | 0.247 |
| | 5 | 0.299 | 0.187 | 0.163 | 0.105 | 0.247 |

| Supplementary Table 2. Key assumptions of model |
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| **Assumptions** |
| Variations in health state utilities over time could only be explained by variations in frequency of OAB symptoms (frequency of micturition and incontinence) and AEs. Urgency had no independent effect in health state utilities. |
| For AEs leading to discontinuation, utilities were reduced from the midpoint of the one month cycle during which the AE occurred. Most patients discontinued treatment at the end of the cycle (i.e., two weeks later) and the AE resolved immediately, but a small number of patients could choose to continue treatment despite having AEs. |
| The average number of micturitions and incontinence episodes within each severity level was the same for both treatments and are constant over time. |
| Discontinuation of treatment could be due to AEs or other reasons. The probability of discontinuation for other reasons was independent of the severity of symptoms, as patients could discontinue for lack of efficacy or because their symptoms had resolved. The rate of discontinuation for other reasons was the same for both treatments. |
| Patients did not receive further drug treatment after stopping mirabegron or tolterodine ER 4 mg, i.e., they were assigned to 'no treatment.' Patients who stopped treatment could reinitiate treatment at a later cycle. |
| The distribution of patients by level of symptom severity after treatment discontinuation was identical to the distribution at baseline. |
| Other than dry mouth and constipation, there was no significant difference in the probabilities of AEs between mirabegron and tolterodine ER 4 mg.[1] |
| The probability of symptom improvement was greatest in the first month following treatment initiation, then decreased progressively and was assumed constant after three months (i.e., the probabilities of transition between severity levels were the same in the fourth and subsequent months as those in the third month). |
| No cost was incurred for primary care visits for prescription renewals, as these were made during routine visits and occurred independently of treatment. |
| Primary care and specialist visits occurred when a new treatment was started (i.e., at initial entry into the model) or restarted. |
| The number of pads per day was derived for each health state and was independent of treatment for a given level of severity. |
| Productivity costs related to absenteeism were dependent upon incontinence severity and were independent of treatment for a given level of severity. Employment rate and annual salary were calculated based on age distribution in the ARIES study.[2] |
| Patients took one tablet per day of mirabegron or tolterodine ER 4 mg, for each day of every month until discontinuation. The analyses did not account for drug wastage or partial compliance. |
| Patients took 50 mg mirabegron or 4 mg tolterodine ER once daily; the dose or formulation did not change over time. |
| The probability of reinitiating drug treatment among patients who previously discontinued was 5.61% (50% annually). All patients were re-initiated with the same treatment that was discontinued if the discontinuation was due to well-managed symptoms or remission of symptoms. |
| The monthly probability of treatment discontinuation among patients with AEs was 90%. |

AE: adverse events; ER: extended release; OAB: overactive bladder.

## References


1. Maman K, Aballea S, Nazir J, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: A systematic literature review and mixed treatment comparison. *Eur Urol* 2014;65:755-65. http://dx.doi.org/10.1016/j.eururo.2013.11.010
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