Patterns of Use of Antimuscarinic Drugs to Treat Overactive Bladder in Denmark, Sweden, and the United Kingdom

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CONFLICT OF INTEREST

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BACKGROUND

- Antimuscarinic drugs have been the only drug class available in Europe to treat overactive bladder (OAB) for many years.
- In late 2012, with the marketing approval of mirabegron, a drug with a new mechanism of action, the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) requested an evaluation of the safety of the new drug.
- This drug utilization study is part of the program designed to meet the FDA's and EMA's requests.[1-3]

OBJECTIVE

- To describe the patterns of use of antimuscarinic drugs to treat OAB in Denmark, Sweden, and the United Kingdom (UK) in the years 2004 to 2012.

METHODS

Study Drugs

- Darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium

Study Design and Data Sources

- Cohort study of adults newly exposed to drugs used to treat OAB in the period from January 1, 2004, through December 31, 2012
- Based on data from Danish and Swedish nationwide registers and the Clinical Practice Research Datalink (CPRD), an electronic medical record database from the UK

Study Population

- Included individuals aged 18 years or older with ≥ 12 months of continuous enrollment followed by a prescription for a study drug, provided that the same agent was not prescribed during the previous 12 months
- Excluded individuals with cancer (except nonmelanoma skin cancer) diagnosed prior to the index prescription and subjects with HIV infection prior to the index prescription in Sweden and the UK

Therapy Episodes

- Concatenated consecutive prescriptions into therapy episodes
- End of episode at no refill, switch to another drug, addition of another antimuscarinic drug, or end of the study period

Statistical Analysis

- Descriptive statistics for characteristics of patients and therapy episodes
- Presented trends in drug use over the study period graphically

RESULTS

- Patient characteristics are shown in Table 1
- **Therapy episodes (Table 2):**
  - Denmark: 4% darifenacin, 9% fesoterodine, 2% oxybutynin, 39% solifenacin, 35% tolterodine, 12% trospium
  - Sweden: 8% darifenacin, 13% fesoterodine, 5% oxybutynin, 35% solifenacin, 37% tolterodine, 3% more than one treatment; trospium was not available
  - UK: 0.3% darifenacin, 3% fesoterodine, 28% oxybutynin, 27% solifenacin, 26% tolterodine, 6% trospium, 10% more than one treatment
- **Time trends in new drug use:**
  - All countries: Decreased new use of tolterodine; increased new use of solifenacin (Figure 1)
  - Sweden: Increased use of fesoterodine
  - UK: Increased use of oxybutynin
- **One prescription:** About half of the episodes in all countries (Table 2)
- **No exposure to any study drug in previous 12 months:** 53% in Sweden; 92% in the UK; not available for Denmark
- **Episode ended because of no refill during study period:** 93% in Demark, 83% in Sweden, 81% in the UK
- **Drug most switched to or added:** Solifenacin in all countries (Table 2); consistent with the upward trend for new use of solifenacin (Figure 1)

DISCUSSION

- Time trends in drug use for tolterodine and solifenacin were similar in the three countries, but not for all other drugs.
- Demographic patient characteristics were similar in the three populations, and patterns of use of the study drugs were generally similar in terms of number of prescriptions per episode and percentages of no refill. Patients in the UK appear to be sicker (e.g., higher prevalence of hypertension based on diagnosis or treatment), but this finding may reflect more complete recording of conditions that do not require hospitalization in the electronic medical records in the UK.
- The main limitation of this study is that in many cases the duration of prescriptions, which was needed to create therapy episodes, was estimated. A limitation specific to the UK is that CPRD only includes prescriptions issued by general practitioners.
- Among the strengths of this study is the use of population-based databases. Our results include practically the entire population of Denmark and Sweden and are expected to be representative of the population of the UK.

CONCLUSIONS

- In these three cohorts of similar age and sex distributions, about half of the episodes consisted of one prescription, and most episodes ended due to no refill.
- The most frequently used drugs were tolterodine and solifenacin, with decreasing use of the former and increasing use of the latter.
- Oxybutynin use was small in the Nordic countries compared with the UK.

ABSTRACTS FROM THIS PROGRAM ALSO PRESENTED IN THIS CONFERENCE

Arana A, et al. **Do individual antimuscarinic drugs to treat overactive bladder have different cardiovascular risks? A UK CPRD cohort study.** Abstract #920. Poster Session C: Safety & Effectiveness - GU & Hormones, Sunday, 28 August 2016, 8:00 AM-1:45 PM.

Fortuny J, et al. **Evaluation of free-text comments to validate common cancer diagnoses in the UK CPRD.** Abstract #91. Poster Session A: Spotlight Session-Databases, Friday, 26 August, 8:00 AM-6:00 PM.

Hallas J, et al. **Incidence of cardiovascular events in new users of overactive bladder medications in Denmark.** Abstract #848. Oral presentation in session CV Adverse Events: Affairs of the Heart, Sunday, 28 August 2016, 3:15 PM-4:45 PM.

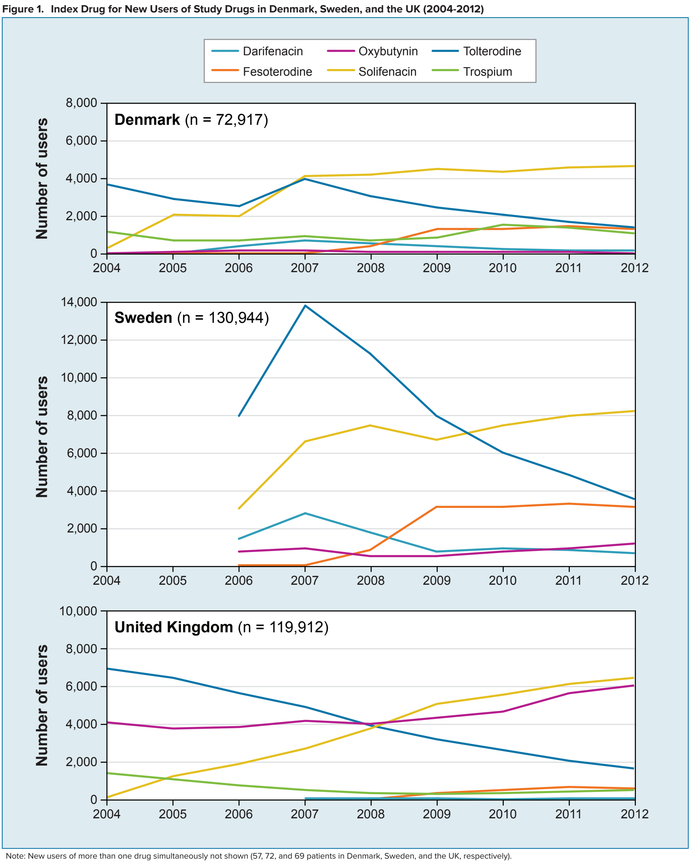
Hallas J, et al. **Elevated bladder and prostate cancer rates following initiation of OAB medication: findings from the Danish registries, 2008-2012.** Abstract #918. Poster Session C: Safe-ty & Effectiveness - GU & Hormones, Sunday, 28 August 2016, 8:00 AM-1:45 PM.

Linder M, et al. **Cancer risk in users of antimuscarinic drugs for overactive bladder: a cohort study in the Swedish national registers.** Abstract #919. Poster Session C: Safety & Effectiveness - GU & Hormones, Sunday, 28 August 2016, 8:00 AM-1:45 PM.

Linder M, et al. **Cardiovascular risk in users of antimuscarinic drugs for overactive bladder: a cohort study in the Swedish national registers.** Abstract #849. Oral presentation in session CV Adverse Events: Affairs of the Heart, Sunday, 28 August 2016, 3:15 PM-4:45 PM.

Margulis AV, et al. **Validation of cardiovascular events and covariates in CPRD GOLD using questionnaires to general practitioners.** Abstract #437. Oral presentation in session Identification and Validation of Outcomes, Saturday, 27 August 2016, 8:00 AM-9:30 AM.

Figure 1. Index Drug for New Users of Study Drugs in Denmark, Sweden, and the UK (2004-2012)



Note: New users of more than one drug simultaneously not shown (57, 72, and 69 patients in Denmark, Sweden, and the UK, respectively).

Table 1. Patient Characteristics by Index Antimuscarinic OAB Drug in Denmark, Sweden, and the UK

Characteristic	Darifenacin	Fesoterodine	Oxybutynin	Solifenacin	Tolterodine	Trospium
Denmark (n = 72,917)						
Patients[a]	4%	8%	1%	42%	33%	13%
Age in years (median)	69	67	66	68	69	68
Female	66%	59%	81%	60%	58%	60%
Hypertension[b]	21%	25%	24%	23%	21%	21%
Diabetes[b]	8%	9%	7%	8%	8%	8%
Smoking[c]	9%	12%	10%	11%	10%	10%
Stroke	13%	13%	16%	14%	16%	14%
Coronary heart disease	6%	6%	5%	6%	6%	5%
Sweden (n = 130,944)						
Patients[a]	7%	10%	4%	36%	42%	n/a
Age in years (mean)	67	65	55	65	68	n/a
Female	63%	60%	63%	64%	55%	n/a
Hypertension[b]	48%	48%	35%	47%	49%	n/a
Diabetes[b]	11%	11%	8%	11%	12%	n/a
Smoking[c]	1%	2%	1%	1%	1%	n/a
Stroke	6%	5%	3%	5%	7%	n/a
Coronary heart disease	11%	10%	7%	9%	10%	n/a
UK (n = 119,912)						
Patients[a]	0.1%	2%	34%	28%	31%	5%
Age in years (mean)	65	60	63	61	63	64
Female	70%	70%	68%	74%	69%	69%
Hypertension[b]	83%	80%	81%	80%	80%	82%
Diabetes[b]	11%	13%	12%	12%	10%	12%
Current smoking	17%	16%	16%	16%	16%	16%
Stroke	10%	7%	7%	6%	7%	8%
Coronary heart disease	17%	12%	13%	12%	13%	15%

n/a = not applicable.
[a] Row percentage (others are column percentages).
[b] Based on diagnosis or treatment.
[c] Smoking in the Nordic countries based on the proxy dispensing of smoking cessation drugs.
Note: 57, 72, and 69 patients entered the cohort on multiple drugs in Denmark, Sweden, and the UK, respectively.

Table 2. Characteristics of Therapy Episodes by Therapy Episode Drug in Denmark, Sweden, and the UK

Characteristic	Darifenacin	Fesoterodine	Oxybutynin	Solifenacin	Tolterodine	Trospium
Denmark						
Prescriptions per episode (over 224,680 total therapy episodes)						
1	43%	49%	51%	46%	54%	50%
2	21%	20%	18%	20%	20%	15%
3	11%	9%	9%	11%	8%	9%
4	7%	6%	6%	6%	4%	5%
≥ 5	19%	16%	17%	17%	15%	21%
Therapy episodes ending in a switch to or an add-on (over 224,680 total therapy episodes)	11%	8%	24%	6%	6%	10%
Sweden						
Prescriptions per index therapy episode (over 130,944 index episodes)						
1	48%	50%	62%	49%	55%	n/a
2	17%	15%	14%	15%	14%	n/a
3	9%	8%	7%	8%	7%	n/a
4	6%	6%	4%	6%	5%	n/a
≥ 5	21%	22%	13%	22%	19%	n/a
Therapy episodes ending in a switch to or an add-on (over 240,141 total therapy episodes)	25%	15%	24%	13%	16%	n/a
UK						
Prescriptions per index therapy episode (over 119,912 index episodes)						
1	41%	46%	56%	46%	50%	52%
2	9%	16%	13%	13%	12%	12%
3	11%	7%	6%	7%	7%	7%
4	4%	5%	4%	5%	4%	4%
≥ 5	36%	27%	21%	30%	28%	25%
Therapy episodes ending in a switch to or an add-on (over 245,800 total therapy episodes)	26%	11%	9%	8%	11%	12%

Note: For Denmark, therapy episodes with multiple drugs are included in the columns for each of the involved drugs. For Sweden and the UK, they are not presented in this table. For Denmark, we present information on number of prescriptions per therapy episode and drugs switched to or added based on all therapy episodes. For Sweden and the UK, we present information on number of prescriptions based on index therapy episodes and drugs switched to or added based on all therapy episodes.

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