

Drug Corner

Assessment of Prescribing Practices in Overactive Bladder Pharmacotherapy across Different Specialties of India : A Prescription Trend Analysis

Vishavadia Krunal¹, Sandip Solanki², Sandesh Warudkar³, Hiren Prajapati⁴, Madhu Sharma⁵

Purpose : To assess the temporal prescription patterns of overactive bladder (OAB) pharmacotherapy based on the prescription trend analysis amongst Indian clinicians.

Methods : IQVIA (Quintiles and IMS Health) secondary sales audit (SSA) and prescription audit for antimuscarinics and beta-3 adrenoceptor agonist (mirabegron) from 2014 to 2022, were analyzed. Prescribers overlap analysis for solifenacin and mirabegron among Indian urologists was also analyzed.

Results : Urologists' prescription rates of OAB drugs were 65% in 2016 and 52% in 2022. The rate of OAB medication prescription by non-urologists was highest among surgeons (17%), followed by consultant physicians (9%) and gynecologists (8%) in 2022. In addition, among OAB medication prescription rates for antimuscarinics were 100% in 2016 and 56% in 2022 whereas for mirabegron, it was 0% in 2016 and 44% in 2022. The proportion of prescribers of OAB medication among urologists was 38% in 2016 and 33% in 2022. Exclusive prescribers of solifenacin were 748 in 2018 and 715 in 2022 at the urologist, whereas for mirabegron, it was 961 in 2018 and 1475 in 2022.

Conclusions : Urologists remained a top prescribing specialty for OAB drugs, although prescription share increased among surgeons and consultant physicians. OAB medicines prescriptions by urologists are shifting from solifenacin to mirabegron. The results of this study could further help clinicians, to design the optimum treatment approach in OAB patients according to their need, which can help to lower antimuscarinic side effects, improves treatment adherence, and improves patient's QoL.

[J Indian Med Assoc 2022; 120(12): 74-9]

Key words : Overactive bladder; Prescription analysis; IQVIA database; Antimuscarinics, Mirabegron.

There are a variety of symptoms associated with an Overactive Bladder (OAB), which include urgency, frequency, and nocturia, with or without Urge Urinary Incontinence (UUI)¹. OAB is also associated with decreased quality of life and a high economic cost to society².

International Continence Society (ICS) estimates that 12.8% of women and 10.8% of men suffer from OAB; the prevalence of frequency, urgency, and Urge Incontinence (UI) rises with age^{3,4}. In Men, UUI was significantly lower than in women. The reported prevalence of OAB in India is 10-42%, with a

progressive increase in prevalence from the third to seventh decade of life⁵.

Behavioural and self-control training methods are regarded as first-line options for reducing urine incontinence in patients. Antimuscarinics or β 3 adrenoceptor agonists are popular treatments for OAB if behavioural changes fail to alleviate symptoms⁶. In India, the most commonly prescribed OAB medications are solifenacin, oxybutynin, tolterodine, darifenacin, trospium, and mirabegron⁷ (Table 1).

Antimuscarinics prevent the contraction of the smooth muscle wall around the bladder. Stimulation of the acetylcholine muscarinic M3 receptors in the detrusor muscle wall usually results in micturition. Solifenacin and darifenacin are muscarinic receptor antagonists that only affect the M3 receptor. Oxybutynin and tolterodine are non-selective antimuscarinics that affect all muscarinic receptors, which causes dry mouth⁹. As a beta-3 agonist, mirabegron relaxes the detrusor muscles and enhances bladder storage capacity without affecting voiding contractions. As a result, mirabegron can assist in alleviating the symptoms of OAB¹⁰. According

¹PhD, Gujarat Technological University, Ahmedabad, Gujarat 382424, India and Corresponding Author

²PhD, Associate Professor, SIB, Pune, Maharashtra 411057, India

³MD, Department of Pharmacology, Maharashtra University of Health Sciences, Nashik, Maharashtra 422004, India

⁴MD, Editorial Board Member, IJDE, Ahmedabad, Gujarat 382470, India

⁵MD, Department of Anaesthesiology, Sardar Vallabhbhai Patel Institute of Medical Science and Research, Ellisbridge, Ahmedabad, Gujarat 380006, India

Received on : 24/11/2022

Accepted on : 30/11/2022

Table 1 — Treatment of Non-Neurogenic Overactive Bladder (OAB) in adults^{1,8}

First-Line Treatments	Behavioral Therapies	Bladder training Bladder control strategies Pelvic floor muscle training Fluid management
Second-Line Treatments	Pharmacologic Management	Antimuscarinic Solifenacin Oxybutynin Tolterodine Darifenacin Trospium Propiverine Fesoterodine Beta-3 adrenoceptor agonists Mirabegron Vibegron Serotonin noradrenaline reuptake inhibitor Duloxetine
Third-Line Treatments	PTNS and Neuro-modulation	Intradetrus oronabotulinumtoxinA (100U) Peripheral tibial nerve stimulation (PTNS) Sacral neuromodulation (SNS)
Fourth-Line Treatments	Augmentation Cystoplasty and Urinary Diversion	Augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB

to a report by the Urological Society of India, OAB is most commonly treated with antimuscarinic or beta-3 adrenoceptor agonists⁵.

The objective of the present study is to assess the prescription pattern of OAB pharmacotherapy especially antimuscarinic and beta-3 adrenoceptor agonists, based on the prescription trend analysis among Indian clinicians.

MATERIALS AND METHODS

Data Source and Setting :

From August 2016 to August 2022, we have been using IQVIA Medical Audit Data (formerly IMS Health) to track the urological preparation prescription rates for primary care physicians in India who work in the private sector¹¹. In more than 100 countries, IQVIA collects market intelligence and disseminates it. Medical audit data monitor prescriptions written by allopathic doctors in private practices. Data were gathered from a random sample of 4600 healthcare practitioners from 23 metropolitan areas of India (over 1 million population), 128 Class 1 cities (population over 100,000), and 1A cities (population fewer than 100,000). A national sample of prescriptions written by doctors in cities with populations greater than one million was drawn from the original data¹².

The data use the European Pharmaceutical Market Research Association's (EphMRA) Anatomical Therapeutic Classification (ATC). The data does not include prescriptions written in the public sector,

thereby analysis only includes outpatient prescriptions from the private sector. Last but not least, IQVIA makes the data available to us in aggregate form, processed, and extrapolated to reflect national prescription practices.

Outcome Measure :

The study focused on the antimuscarinics (solifenacin, oxybutynin, tolterodine, darifenacin, and trospium) and mirabegron prescribed each year as a primary outcome measure. In addition, a study estimated and reported prescriptions by specialty and molecule.

Statistical Analysis :

The study used the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, to code prescription diagnosis data from an IQVIA medical audit (ICD-10 classification; version: 2016)¹². Anatomic

Therapeutic Chemical (ATC) classification of antimuscarinics and beta-3 adrenoceptor agonists recommended for the related diagnosis have been coded to the 3rd level of WHOCC's proposed drug statistics methodology (ATC index-2016)¹³. Based on the diagnostic information provided, medical audit data was used to code the ICD 10 at the smallest level possible.

The annual prescription data of IQVIA medical audit for urological preparations, including antimuscarinics and beta-3 adrenoceptor agonists, were analyzed. The medicines prescribed were categorized into these subgroups: solifenacin, darifenacin, tolterodine, oxybutynin, trospium & mirabegron. We used software Microsoft Excel 2013 to perform statistical analysis.

Ethics Considerations :

The data used had no identifiers for the patients. So current study does not require Ethical Committee approval.

RESULTS

Prescription and prescriber data of various antimuscarinics and beta-3 adrenoceptor agonists were analyzed for 7 Moving Annual Total (MAT) periods starting from MAT Aug'16 to MAT Aug '22.

In 2016, for OAB treatment, 84% of prescriptions were generated by the top 4 specialties, ie, urologist, consultant physician, gynecologist & general surgeon, which further increased to 86% in 2022. In MAT 2022, the urologist is the leading specialty prescribing OAB

drugs, with a 52% prescription share. General surgeon contributes 17%, while consultant physician and gynaecologist have a 9% & 8% prescription share, respectively (Fig 1A).

In 2016, 38% of urologists contributed 65% of prescriptions in the OAB drug market, which reduces to 33% and 52% in 2022, prescriber contribution and prescription contribution, respectively. At consultant physicians, prescriber contribution increases from 11% to 17%. Still, at the same time, prescription contribution did not grow at the same pace (6% to 9%), mainly because of low prescription per doctor per month (PDM). 8% of surgeons contributed around 5% of prescriptions in 2016, which increased to 17% in 2022 due to a positive change in the number of prescriptions per doctor (Fig 1B).

Antimuscarinics and beta-3 adrenoceptor agonist, mirabegron are the preferred drugs for the medical management of overactive bladder in India. Prescription share for antimuscarinics were 100% in 2017 & 56% in 2022 whereas for mirabegron, it was 0% in 2017 & 44% in 2022. Prescriber share data also reflect a similar trend, antimuscarinics were 100% in 2017 & 64% in 2022 whereas, for mirabegron, it was 0% in 2017 & 36% in 2022 (Fig 2).

Before the launch of Mirabegron in the Indian market, solifenacin was the most preferred drug for the treatment of OAB, with a prescription share of 37% in 2017. Mirabegron was approved in India by Central Drugs Standard Control Organisation (CDSCO) in June 2017 & marketed by Nov 2017¹⁴. The majority of Antimuscarinics lost their prescription share to mirabegron, as in 2022, mirabegron gained 44% prescription share in the OAB market (Table 2).

Solifenacin prescription share reduced from 36% to 30%, during 2016-2022. Major loss in prescription share for antimuscarinics was, oxybutynin (19% - 8%), tolterodine (18% - 9%), and darifenacin (25% - 9%). MAT 2020 period experienced COVID-19 impact in terms of loss in prescription, applicable to all the molecules. Greater relative prescription loss at antimuscarinics indicates the change in molecular preference in OAB management.

Among different specialties, urologists were the major specialty prescribing overactive bladder drugs & solifenacin was the most preferred molecule (38% prescriber share) in India before the launch of mirabegron. Tolterodine was the second preferred drug (29% prescriber share) for OAB by urologists in 2016, but in 2022, the prescriber share was reduced to 12%. Darifenacin also lost the prescriber share from 18% to 4% (Fig 3).

OAB medication preferences by urologists are shifting from antimuscarinics to mirabegron. Other specialties continue to prescribe antimuscarinics as a preferred drug for OAB (Fig 4).

Solifenacin and mirabegron are the most prescribed molecules across specialties and also by urologists. An exclusive prescriber (urologist) based analysis was done to understand the molecular shift at the prescriber level.

In India, before the launch of mirabegron, solifenacin dominated the OAB market. But after the launch of mirabegron, a considerable decline was observed in solifenacin prescribers and a significant gain in mirabegron prescribers. The decline in solifenacin exclusive prescribers and gain in mirabegron exclusive prescribers show the molecular shift at the urologist level from solifenacin to mirabegron.

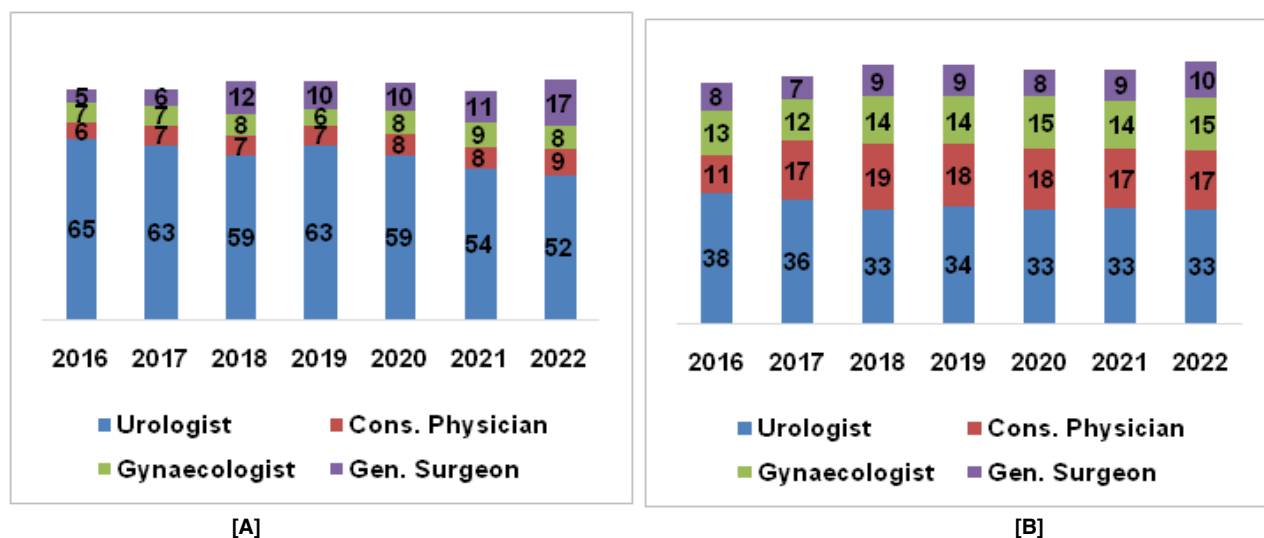


Fig 1 — Speciality-wise contribution for OAB drugs in India (2016-2022) : [A] Prescription share; [B] Prescriber contribution

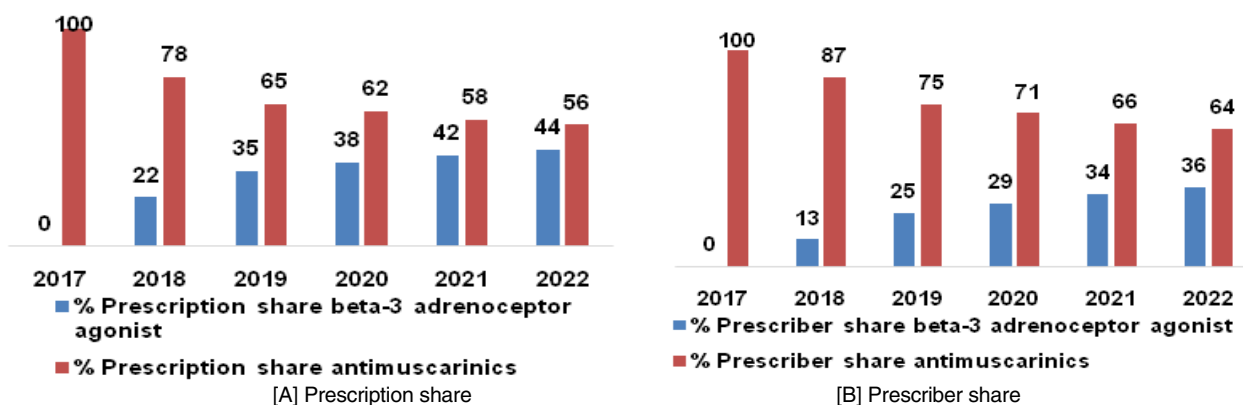


Fig 2 — % Prescription and Prescriber share of beta-3 adrenoceptor agonist and antimuscarinics (2017-2022)

Drugs for OAB	2016	2017	2018	2019	2020	2021	2022
Mirabegron	0	0	22	35	38	42	44
Solifenacin	36	37	28	31	33	33	30
Oxybutynin	19	20	17	12	10	7	8
Tolterodine	18	19	15	9	10	9	9
Darifenacin	25	21	17	13	9	9	9
Trospium	2	2	1	1	0	0	0

DISCUSSION

The urology drug market contributes almost 1.6% to the Indian pharmaceutical market. Drugs for OAB contribute 7.3% of the total urology market. Although the prevalence of OAB in India ranges from 10 - 42%¹⁵, the market size is minuscule, just 0.1% in the Indian pharmaceutical market¹⁵.

Among Indian urologists, solifenacin (46.7%) is the most commonly prescribed drug for UUI, according to a survey conducted by the Urological Society of India (November 2017). In the two months following the launch of mirabegron in India, a 4.5% preference for mirabegron was recorded¹⁶.

The efficacy and tolerability data unveil the reason behind shifting the molecular preference of Indian clinicians within the antimuscarinics or antimuscarinics to mirabegron. Many studies have compared the efficacy and tolerability of antimuscarinics/solifenacin vs. mirabegron. The majority of studies concluded antimuscarinics/solifenacin are comparable with mirabegron in efficacy, but mirabegron scores more on tolerability and thereby therapy adherence¹⁷⁻¹⁹.

Solifenacin 5 mg/day was found to be as effective as other common antimuscarinics across the spectrum of OAB symptoms and more effective than tolterodine 4 mg/day in reducing incontinence and UUI episodes, according to a systematic review and meta-

analysis. When compared to other solifenacin doses, such as 10 mg/day, darifenacin 15 mg/day, tolterodine IR 4 mg/day, fesoterodine 8 mg/day, propiverine 20 mg/day, and oxybutynin (IR 9-15 mg/day or ER 10-mg-daily), solifenacin 5 mg/day had a lower incidence of dry mouth²⁰.

Mirabegron is an oral adrenoceptor agonist that provides an alternative to antimuscarinics for patients with OAB, as phase III trials of mirabegron versus placebo found significant improvements in key efficacy measures (eg, urinary incontinence and frequency of urination)¹⁷. Researchers compared antimuscarinics and mirabegron 50mg in patients with OAB by conducting a systematic literature review and network meta-analysis based on peer-reviewed articles published between 2000 and 2013. Mirabegron 50 mg was as effective as antimuscarinics (excluding solifenacin 10 mg) for urinary frequency, incontinence, and UUI episodes, according to 44 RCTs involving 27,309 patients²¹. Also, mirabegron was found to be better tolerated in terms of dry mouth, constipation, and urinary retention than antimuscarinics.

Better symptomatic relief with patient satisfaction is the primary objective behind any medical treatment.

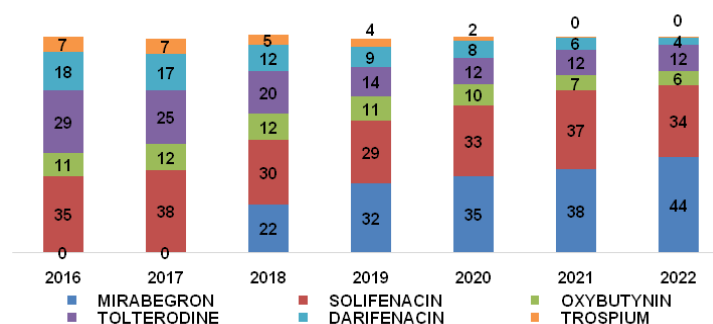


Fig 3 — Prescriber share of OAB drugs at Urologist specialty (2016-2022)

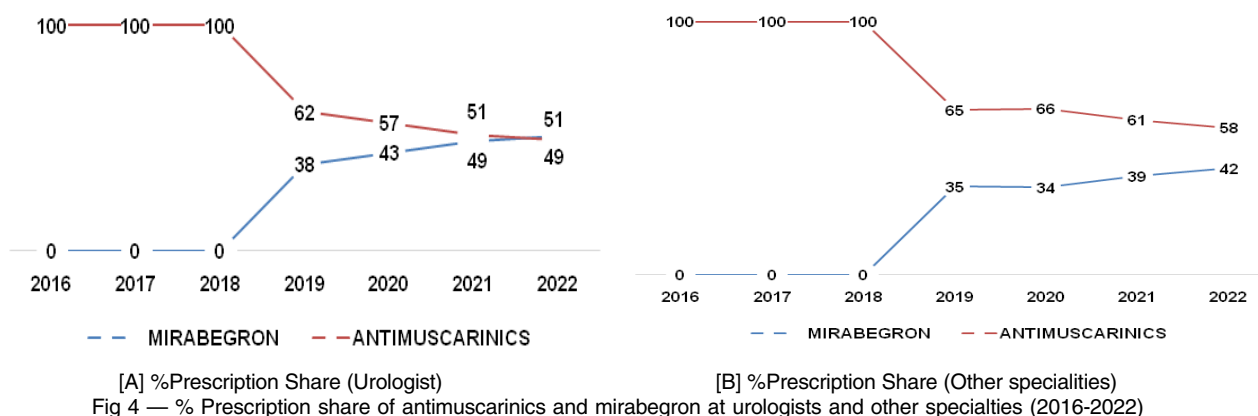


Fig 4 — % Prescription share of antimuscarinics and mirabegron at urologists and other specialties (2016-2022)

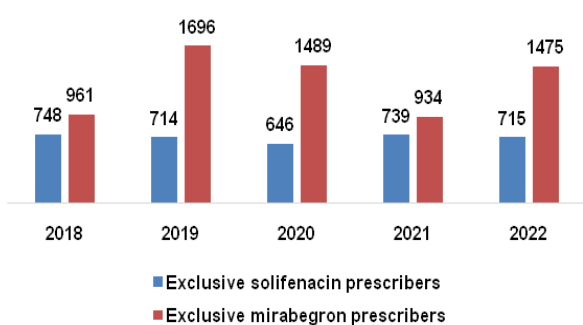


Fig 5 — Exclusive prescriber (urologist) analysis for Solifenacin and Mirabegron

Antimuscarinics fulfil the first requirement and provide better symptom relief, but patient satisfaction is less due to undesirable side effects. Patients switching from antimuscarinics to mirabegron for OAB have better outcomes if their baseline OAB symptom scores are higher, such as the OAB-SS and IPSS-S²². According to a retrospective cohort study, Mirabegron may reduce the antimuscarinic drug's dosage and thus improve NDO treatment's long-term efficacy²³. High therapy adherence, comparable efficacy, and lower side effects could be why clinicians shift their preference from solifenacin to mirabegron.

Recently CDSCO has approved a fixed-dose combination of solifenacin and mirabegron²⁴. The randomized, multicentre SYNERGY trial studied the long-term safety and efficacy of the combination of mirabegron and solifenacin in patients with overactive bladder compared to monotherapy. The study concluded that the treatment with a combination of solifenacin and mirabegron was better tolerated and found to be effective than solifenacin monotherapy²⁵. In the Indian market, the mirabegron/solifenacin combi pack was introduced in late 2019, whereas the fixed-dose combination was approved in 2021²⁶.

OAB is a common disease that causes serious problems such as UTIs, skin infections, bladder

stones, falling/fractures in the elderly, sleep disturbances, adverse effects on quality of life, and depression²⁷. OAB is often accompanied by chronic diseases such as hypertension and diabetes. It is common for elderly incontinence patients to be managed by a non-urologist, especially in rural areas²⁸. Urologists were most likely to prescribe mirabegron whereas non-urologists were found to prescribe older-generation antimuscarinics like oxybutynin and darifenacin; rather than a newer class of OAB drug, mirabegron²⁹.

Limitation :

Our study is not deprived of limitations. The IQVIA database did not offer detailed, patient-level data on OAB management; only limited OAB data could be included in this study, representing a source of bias. Moreover, IQVIA data were extrapolated to a population of Indian physicians using inverse proportional weight. In doing this, it is assumed that the stable panel generally represents other practices, pharmacies, and hospitals for which IQVIA did not have reliable data. Minor difference in the stable panel creates significant differences in the final data output. Also, the current study only evaluates prescriptions and prescriber trends of two major classes of drugs, ie, antimuscarinics and beta-3 adrenoceptor agonists used for the treatments of OAB. No other pharmacotherapy has been evaluated. Despite limitations, our study comprehensively evaluated the change in practicing trends of OAB management.

Conclusion :

Urologists remained a top prescribing specialty for OAB drugs, although prescription share increased among surgeons and consultant physicians. OAB medication preferences by urologists are shifting from solifenacin to mirabegron. Other non-urologist specialties continue to prescribe antimuscarinics as a preferred drug for OAB. Antimuscarinics' prescription

share shows a downtrend due to the risk of side effects and lowers therapy adherence compared with mirabegron, which is comparatively better tolerated & equally effective in OAB management. Across Indian specialties, mirabegron emerges as a promising treatment option for overactive bladder. Recently approved fixed-dose combination of antimuscarinic, solifenacin, and beta-3 adrenoceptor agonist mirabegron is the newer approach for refractory OAB management in India. Results of this study could further help clinicians, to design the optimum treatment approach in OAB patients according to their need, which can help to lower antimuscarinic side effects, improves treatment adherence, and improves patient's quality of life.

Ethics approval and consent to participate :

The data we used had no identifiers for the patients. We, therefore, did not require ethical approval for our study.

Funding : The authors received no specific funding for this work.

Competing interests : The authors have declared that no competing interests exist.

REFERENCES

- Wróbel A — Overactive bladder syndrome pharmacotherapy: future treatment options, *Menopausal Rev* 2015; **4(4)**: 211-7.
- Lee UJ — Defining and Managing Overactive Bladder: Disagreement Among the Experts. *Urology* 2013; **81(2)**: 257-62.
- Irwin DE — Population-Based Survey of Urinary Incontinence, Overactive Bladder, and Other Lower Urinary Tract Symptoms in Five Countries: Results of the EPIC Study. *Eur Urol* 2006; **6**: 1306-5.
- Moorthy P, Lapitan MC, Quek PLC, Lim PHC — Prevalence of overactive bladder in Asian men: an epidemiological survey. *BJU Int* 2004; **93(4)**: 528-31.
- Sinha S — The urological society of India guidelines for the evaluation and management of nonneurogenic urinary incontinence in adults (executive summary). *Indian J Urol* 2019; **35(3)**: 185-8.
- Gulur DM, Drake MJ — Management of overactive bladder. *Nat Rev Urol* 2010; **7(10)**: 572-82.
- Central Drugs Standard Control Organization, "CDSCO List of Approved New Drugs," 2021. [Online]. Available: https://cdsco.gov.in/opencms/opencms/en/Approval_new/Approved-New-Drugs/. [Accessed: 03-Jun-2021].
- Gormley EA — Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol* 2012; **188(6)**: SUPPL 2455-63.
- Chilman Blair K, Bosch JL — Solifenacin: Treatment of overactive bladder. *Drugs of Today* 2004; **40(4)**: 343.
- Mandpe P, Prabhakar B, Shende P — Potential of Mirabegron and its Extended-release Formulations for the Treatment of Overactive Bladder Syndrome. *Curr Drug Metab* 2020; **21(2)**: 79-88.
- Candore G, Hedenmalm K, Slattery J, Cave A, Kurz X, Arlett P — Can We Rely on Results From IQVIA Medical Research Data UK Converted to the Observational Medical Outcome Partnership Common Data Model? *Clin Pharmacol Ther* 2020; **107(4)**: 915-25.
- Farooqui HH, Mehta A, Selvaraj S — Outpatient antibiotic prescription rate and pattern in the private sector in India: Evidence from medical audit data," *PLoS One* 2019; **14(11)**: 1-11.
- WHO, "International Statistical Classification of Diseases and Related Health Problems (ICD)," 2016. [Online]. Available: <https://icd.who.int/browse10/2016/en>. [Accessed: 09-Jun-2021].
- CDSCO — Recommendations of the SEC (Reproductive & Urology) made in its 25. 2017; 6-8.
- IQVIA India — IQVIA Industry Highlights AUG-20. *IQVIA Inst Hum Data Sci* 2020; 5.
- Sinha S — The Urological Society of India survey on urinary incontinence practice patterns among urologists. *Indian J Urol* 2018; **34(3)**: 202-10.
- Kelleher C — Efficacy and Tolerability of Mirabegron Compared with Antimuscarinic Monotherapy or Combination Therapies for Overactive Bladder: A Systematic Review and Network Meta-analysis. *Eur Urol* 2018; **74(3)**: 324-33.
- Yeowell G, Smith P, Nazir J, Hakimi Z, Siddiqui E, Fatoye F — Real-world persistence and adherence to oral antimuscarinics and mirabegron in patients with overactive bladder (OAB): a systematic literature review. *BMJ Open* 2018; **8(11)**: e021889.
- Chapple CR — Persistence and Adherence with Mirabegron versus Antimuscarinic Agents in Patients with Overactive Bladder: A Retrospective Observational Study in UK Clinical Practice. *Eur Urol* 2017; **72(3)**: 389-99.
- Nazir J — Comparative efficacy and tolerability of solifenacin 5 mg/day versus other oral antimuscarinic agents in overactive bladder: A systematic literature review and network meta-analysis. *NeuroUrol. Urodyn* 2018; **37(3)**: 986-96.
- Maman K — 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(4)**: 755-65.
- Liao C-H, Kuo H-C — High satisfaction with direct switching from antimuscarinics to mirabegron in patients receiving stable antimuscarinic treatment. *Medicine (Baltimore)* 2016; **95(45)**: e4962.
- Krebs J, Pannek J, Rademacher F, Wöllner J — Real-World Effects of Mirabegron in Patients with Chronic Neurogenic Detrusor Overactivity – A Retrospective Cohort Study," *Res. Reports Urol* 2020; **12**: 187-92.
- CDSCO — Recommendations of the SEC (Reproductive & Urology) made in its 59th meeting. *Cent Drugs Stand Control Organ* 2021; 6-8.
- Gratzke C — Long-term Safety and Efficacy of Mirabegron and Solifenacin in Combination Compared with Monotherapy in Patients with Overactive Bladder: A Randomised, Multicentre Phase 3 Study (SYNERGY II). *Eur Urol* 2018; **74(4)**: 501-9.
- Medical Dialogues Team, "MSN laboratories gets CDSCO panel nod for FDCs Solifenacin, Mirabegron capsules," www.medicaldialogues.in, 2022. [Online]. Available: <https://medicaldialogues.in/news/industry/pharma/msn-laboratories-gets-cdsco-panel-nod-for-fdcs-solifenacin-mirabegron-capsules-90712?infinite-scroll=1>.
- Alana Biggers MD — Overactive Bladder (OAB) Complications," *Healthline*, 2017. [Online]. Available: <https://www.healthline.com/health/overactive-bladder-complications>.
- Liu R-T — Prevalence of Overactive Bladder and Associated Risk Factors in 1359 Patients With Type 2 Diabetes. *Urology* 2011; **78(5)**: 1040-5.
- Sripad AA, Raker CA, Sung VW — Overactive bladder medication: Anticholinergics versus mirabegron by specialty. *Urol J* 2022; 039156032210769.