

## Can We Improve Management of Overactive Bladder in Long-Term Care? *Examining the Role of Beta-3 Adrenergic Agonists*

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### Disclosures

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### Our Goals for Today

- Recognize the scope of burdens that OAB represents in the LTC setting
- Understand why and how to screen patients for OAB, and distinguish OAB from other urinary conditions
- Implement individually appropriate OAB management plans that are effective and safe for people with multiple health concerns

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**Defining Our Terms: What is Overactive Bladder (OAB)?<sup>1,2</sup>**

- "OAB is a clinical diagnosis characterized by the presence of bothersome urinary symptoms"
- Hallmark symptom: **urinary urgency**
  - Defined by the International Continence Society as "sudden, compelling desire to pass urine which is difficult to defer"
- Usually accompanied by **frequency** and **nocturia**
- **With or without urgency urinary incontinence** (ie, "wet" or "dry" OAB)
- In the absence of urinary tract infection or other obvious pathology (eg, excludes neurogenic bladder conditions)

1. Lightner DJ et al. J Urol. 2019;202:559-563. 2. Haylen BT et al. Neurourol Urodyn. 2010;29:4-20.

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**How Common Is OAB?<sup>1-3</sup>**

- Prevalence estimates range from 9%-43% in women and 7%-27% in men
  - OAB definitions, populations, and methodologies vary across these population-based studies of community-dwelling adults

	NOBLE	EpiLUTS <sup>a</sup>	OAB-POLL <sup>a</sup>
Women	16.9%	43% sometimes 33% often	30% sometimes 20% often
Men	16.0%	27% sometimes 16% often	16.4% sometimes 8% often

<sup>a</sup> sometimes or "often" experienced symptoms.  
1. Stewart WF et al. World J Urol. 2003; 20:327-336. 2. Coyne KS et al. Urology. 2011;77:1081-1087. 3. Coyne KS et al. Neurourol Urodyn. 2013;32:230-237.

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### How Common is OAB?<sup>1,2</sup> (Cont'd)

- NOBLE findings indicate that overall prevalence is comparable in men and women (16.0% vs 16.9%), but men with LUTS are often misdiagnosed with BPH
  - Historically, irritative and obstructive symptoms were both attributed to BPH, but irritative symptoms are more likely due to OAB
  - A large claims-based study (N = 462,400 men with LUTS) found potential undertreatment of OAB and misdirection of therapy for men with a combination of voiding and storage symptoms
- Prevalence increases with age
  - More than half of women aged 40-45 years, and more than 85% of women aged 71-75 years, report symptoms of OAB

1. Burnett AL et al. *Neur Urologj*. 2020;39:1375-1386. 2. Coyne KS et al. *Urology*. 2011;77:1081-1087. PeerView.com

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### Burdens of OAB<sup>1,2</sup>

- Negative effects on self-esteem, sexuality, personal relationships, and sense of health
- Associated with elevated levels of anxiety, depression
- Disrupted sleep
- 39% of women with OAB reported that it interfered with ADL
  - 12% stayed at home due to symptoms
  - 38% reported decreased physical activity; 34% attributed weight gain due to inability to exercise
- Associated with higher incidence of falls/fractures in elderly patients

1. Reynolds WS et al. *Curr Bladder Dysfunct Rep*. 2016;11:8-13. 2. Caplan ED et al. *Arch Gerontol Geriatr*. 2016;75:44-50. PeerView.com

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### Comorbidities Contributing to OAB Risk

<div style="background-color: #2c5e8c; color: white; padding: 5px; border-radius: 10px; margin-bottom: 10px;"> <input checked="" type="checkbox"/> <b>Miscellaneous</b> </div> <ul style="list-style-type: none"> <li>• Heart failure<sup>2,3</sup></li> <li>• Nocturia<sup>4</sup></li> <li>• Sleep apnea<sup>2</sup></li> </ul>	<div style="background-color: #8b2323; color: white; padding: 5px; border-radius: 10px; margin-bottom: 10px;"> <input checked="" type="checkbox"/> <b>Psychiatric conditions<sup>5</sup></b> </div> <ul style="list-style-type: none"> <li>• Depression</li> </ul>
<div style="background-color: #8e44ad; color: white; padding: 5px; border-radius: 10px; margin-bottom: 10px;"> <input checked="" type="checkbox"/> <b>Neurologic disease<sup>2</sup></b> </div> <ul style="list-style-type: none"> <li>• Stroke</li> <li>• Parkinson's disease</li> <li>• NPH</li> </ul>	<div style="background-color: #27ae60; color: white; padding: 5px; border-radius: 10px; margin-bottom: 10px;"> <input checked="" type="checkbox"/> <b>Dementia<sup>6-8</sup></b> </div> <ul style="list-style-type: none"> <li>• Alzheimer's disease</li> <li>• Multi-infarct/vascular</li> <li>• Lewy body dementia</li> <li>• Parkinson's disease</li> <li>• Frontotemporal</li> </ul>

1. DeVore EE et al. *J Urol*. 2012;188:1816-1821. 2. <http://www.ncbi.nlm.nih.gov/pubmed/25151000>. 3. Palmer MH, Busby-Whitehead J. *Curr Bladder Dysfunct Rep*. 2015;10:22. 4. Parkhouse RJ, et al. *PLoS One*. 2012;7:e35995. 5. Nief FD, Walling AD. *Am Fam Physician*. 2006;73:1223-1229. 6. Ransmayr GN et al. *Neurology*. 2008;70:299-303. 7. Sakakibara R et al. *J Neurol Neurosurg Psychiatry*. 2005;76:729-732. 8. Averbach MA et al. *Neurourol Urologj*. 2015. PeerView.com

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**Comorbidities Compound OAB Costs<sup>1</sup>**

- Costs accelerate when OAB is comorbid with dementia, depression, T2DM, HTN, and osteoporosis
  - A claims-based study (N = >110,000 pairs of patients with chronic conditions +/- OAB) found that OAB was associated with healthcare costs >2.5 times ( $P < .0001$ ) those of similar patients without OAB ( $P < .0001$ )
  - Synergy of OAB + comorbidities adds ~\$95-\$574 per patient per month to healthcare costs

1. Durlin E et al. Neurolog Urology. 2018;37:1641-1649.

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**OAB in Nursing Homes<sup>1,2</sup>**

- As many as 50%-70% of nursing home residents have UI, which may be OAB-related
- In a claims-based study, nursing home residents with OAB and/or UI had a higher prevalence of depression (47.7% vs 32.4%), cerebrovascular incidents (20.4% vs 10.4%), and dementia (40.8% vs 35.4%) compared with residents without OAB and/or UI
- In 2000, direct cost of OAB in nursing homes was estimated at \$3.5 billion/year
  - Includes diagnosis, treatment, routine care, and health-related consequences (eg, falls, skin conditions, UTI)

1. Aparasu RR et al. Adv Ther. 2020;37:3584-3605. 2. Hu TW et al. Urology. 2004;63:461-465.

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**OAB in LTC: Perspectives From Directors of Nursing<sup>1</sup>**

- Web-based survey among DON (N = 71, each representing a US facility with a mean of 115 residents)
- Findings
  - 65%-70% of residents ≥65 years of age lack complete control of bladder function
  - Approximately 89% of LTC residents need some assistance with toileting
- Caregiver burden surrounding OAB and UI contributes to staff turnover, especially among CNAs
  - CNAs spend an average of 56% of a shift managing UI needs, including changing an average of 37 UI products and assisting with 25.5 toileting episodes

1. Stefanacci RG et al. J Gerontol Nursing. 2022;48:38-46.

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**OAB in LTC: Perspectives From Directors of Nursing<sup>1,2</sup> (Cont'd)**

- 36% of falls in LTC facilities occur when residents are trying to get to a bathroom
  - Increase post-fall meetings, documentation, changes in care plans
- Increases in falls, UTIs, and pressure ulcers affect CMS quality measures
- Monthly costs of urinary incontinence products average \$5400 per facility; rated high relative to other supply costs by 56% of DON
  - Monthly laundry costs related to UIL \$5,500

1. Stefanacci RG et al. J Gerontol Nurs. 2022;48:38-46. 2. Florence CS et al. J Am Geriatr Soc. 2018;66:693-698.

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**Opportunities for Improvement<sup>1</sup>**

- Recognizing and effectively addressing OAB in LTC residents offers an opportunity to:
  - Improve patient quality of life, outcomes, and satisfaction
  - Reduce risk for fall, UTI, skin irritation/infections due to exposure to urine
  - Reduce staff burden, time, and costs
  - Improve all aspects of an LTC facility's quadruple aim:
    - Patient experience, patient outcomes, clinician experience, cost of care

1. Stefanacci RG et al. J Gerontol Nurs. 2022;48:38-46.

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**Routine OAB Screening and Timely Diagnosis in LTC**

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### Diagnostic Basics According to the AUA/SUFU Guidelines<sup>1,2</sup>

- In 2012, the American Urological Association (AUA) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) issued guidelines for diagnosis and treatment of non-neurogenic OAB in adults
  - Amended in 2019, but diagnostic guidance did not change
- Minimum requirements for diagnosis
  - Careful history
  - Physical exam
  - Urinalysis

1. Gormley EA et al. J Urol. 2012;188(6 suppl):2455-2463. 2. Lightner DJ et al. J Urol. 2019;202:558. PeerView.com

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### Elements of the History<sup>1-3</sup>

- Ask about bladder storage symptoms and bladder emptying
  - Sense of urgency can be subjective; ask patients if they have trouble getting to a toilet in time (assuming adequate mobility)
  - Ask about fluid intake—how much and whether caffeinated
- Review comorbidities and medications
  - Medications that can affect bladder function include first generation H<sub>1</sub> receptor agonists, ACE inhibitors, alpha blockers, diuretics, antidepressants, antipsychotics, calcium channel blockers
- Ask how bothersome the symptoms are
  - Is the patient avoiding certain activities due to OAB?
- Validated screening tools can help assess symptoms and bother

1. Gormley EA et al. J Urol. 2012;188(6 suppl):2455-2463. 2. Vorhamme K et al. Drug Saf. 2009;31:373. 3. Zryzrynski H et al. Urinary Incontinence in Women. American Urologic Society PocketGuide. 2012. <http://guideline.guideincontinence.com/76622-augs-urinary-incontinence/67> PeerView.com

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### Validated Screening Tools<sup>1-3</sup>: OAB-V8 and OAB-V3

**OAB-V8: Overactive Bladder-Validated 8-Question Screener**

How Bothered Have You Been By:	Not At All	A Little Bit	Somewhat	Quite a Bit	A Great Deal	A Very Great Deal
1. Frequent urination during the daytime hours?	0	1	2	3	4	5
2. An uncomfortable urge to urinate?	0	1	2	3	4	5
3. A sudden urge to urinate with little or no warning?	0	1	2	3	4	5
4. Accidental loss of small amounts of urine?	0	1	2	3	4	5
5. Nighttime urination?	0	1	2	3	4	5
6. Waking up at night because you had to urinate?	0	1	2	3	4	5
7. An uncontrollable urge to urinate?	0	1	2	3	4	5
8. Urine loss associated with a strong desire to urinate?	0	1	2	3	4	5

Are you male?  If male  add 2 points to your score

Please add up your responses to the questions above  Please hand this page to your doctor when you see him/her for your visit.

If your score is 8 or greater, you might have overactive bladder. There are effective treatments for this condition. You might want to talk with a healthcare professional about your symptoms.

The questions in this table ask about how bothered you may be by some bladder symptoms. Some people are bothered by bladder symptoms and might not realize that there are treatments available for their symptoms. Please circle the number that best describes how much you have been bothered by each symptom. Add the numbers together for a total score, and record the score in the box provided at the bottom.

1. Maltz S et al. Neurol Urologyn. 2020;39:1524. 2. Basra RK et al. J Obstet Gynaecol. 2012;32:666-671. 3. Angulo JC et al. Actas Urol Esp. 2017;41:383-390. PeerView.com

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### Validated Screening Tools<sup>1-4</sup>: Bladder Control Self-Assessment Questionnaire (B-SAQ)

- Encompasses wider range of LUTS symptoms
- Highlights "red flag" symptoms
  - Blood in urine
  - Difficulty passing urine
  - Pain during urination

Question Score	This Question Score Means	This Question Score Means	Other Score
0	You have no urinary symptoms at all	You are completely symptom-free	0.0
0.2	You have very mild symptoms	You are slightly symptomatic	0.2
0.4	You have mild symptoms	You are moderately symptomatic	0.4
0.6	You have moderate symptoms	You are moderately symptomatic	0.6
0.8	You have significant symptoms	Your symptoms are significant	0.8
10.0	You have very significant symptoms	Your symptoms are very significant	10.0

<sup>1</sup> Masde S et al. *Neurourol Urodyn.* 2020;39:13-24. <sup>2</sup> Basra RK et al. *J Obstet Gynaecol.* 2012;32:666-671. <sup>3</sup> Angulo JC et al. *Actas Urol Esp.* 2017;41:383-390.  
<sup>4</sup> Adapted from Basra RK et al. *European Urology.* 2007; 52:230-238.

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### AUA/SUFU Diagnostic Basics<sup>1</sup>

**Physical exam**

- Should include an abdominal exam, a rectal/genitourinary exam, and assessment of lower extremities for edema

**Urinalysis**

- Rule out UTI and hematuria

<sup>1</sup> Gornley EA et al. *J Urol.* 2012;188(suppl):2455-2463.

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### AUA/SUFU Guidelines for OAB Diagnosis: Additional Measures<sup>1</sup>

- Additional steps that might be necessary in some patients to validate an OAB diagnosis, exclude other disorders, or inform treatment planning
  - Urine culture
  - Postvoid residual
    - In patients with obstructive symptoms, history of incontinence/prostatic surgery, neurologic diagnoses
  - Bladder diaries (fluid intake, voiding behavior), symptom questionnaires
    - Useful in patient education, to document baseline, to quantify bladder symptoms, and assess treatment efficacy

<sup>1</sup> Gornley EA et al. *J Urol.* 2012;188(suppl):2455-2463.

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### Differential Diagnosis<sup>1</sup>

#### OAB is considered a diagnosis of exclusion

- Differential can include:
  - Nocturnal polyuria
  - Polydipsia
  - Diabetes insipidus
  - UTI
  - Interstitial cystitis
  - Urinary retention
  - Atrophic vaginitis

1. Lightner DJ et al. J Urol. 2019;202:558-563.

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### American Urogynecologic Society: Watch for DIAPPERS

- D** Delirium
- I** Infection
- A** Atrophic vaginitis
- P** Pharmaceuticals
- P** Psychological
- E** Excess urine output
- R** Reduced mobility
- S** Stool impaction

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### AUA/SUFU Guidelines for Diagnosis: What NOT to Do<sup>1</sup>

#### Initial workup of an uncomplicated patient

- Do not use urodynamics, cystoscopy, or diagnostic renal and bladder ultrasound

#### In complicated or refractory patients

- Choice of additional diagnostic tests depends on patient history, QoL, and clinician judgment

1. Gormley EA et al. J Urol. 2012;188(suppl):2455-2463.

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# OAB Management in the Elderly Population

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### Treatment Continuum<sup>1-3</sup>

**First Line: Lifestyle Changes and Behavioral Therapy**

- Weight loss
- Dietary and fluid management (including limits on caffeine consumption)
- Smoking cessation
- Bowel regularity
- Scheduled voiding
- Bladder training with urge suppression strategies
- Pelvic-floor muscle training (sometimes augmented with biofeedback)

1. Brucker BM et al. Urology. 2020;145:52-59. 2. Lightner DJ et al. J Urol. 2019;202:558-563. 3. Gormley EA et al. J Urol. 2012;188(suppl):2456-2463.

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### Limitations of Lifestyle and Behavior Changes<sup>1</sup>

- *In general*
  - These changes require considerable commitment of patient's time and effort, as well as clinician time for training of patients
  - Adherence and persistence are low
- *In LTC settings*, the high prevalence of patients with OAB and UI make these changes even more challenging
  - Many facilities rely instead on incontinence products and bedding changes rather than bladder retraining
- Some evidence suggests that initiating drug therapy simultaneously with behavioral therapy can improve outcomes

1. Brucker BM et al. Urology. 2020;145:52-59.

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**Treatment Continuum<sup>1</sup>**  
**Second Line: Pharmacotherapy**

- Goal of medical therapy: Reduce uncontrolled bladder contractions
- OAB pathophysiology is not yet fully understood, but multiple theories focus on detrusor overactivity, defined by the ICS as “characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked”

1. Scammell J et al. Exp Ther Med. 2021;22:1444. PeerView.com

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**Treatment Continuum<sup>1</sup>**  
**Second Line: Pharmacotherapy (Cont'd)**

Bladder function depends on a complex mechanism of interactions between the central and peripheral nervous systems

- The parasympathetic nervous system (S2, S3, and S4) coordinates the intensity of detrusor contractions
- The sympathetic component comes from the hypogastric nerve, acts on beta receptors, and is responsible for relaxing the detrusor

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**Two Drug Classes Target the Detrusor to Reduce OAB Symptoms<sup>1-5</sup>**

**Antimuscarinics**

- Block M<sub>2</sub> and M<sub>3</sub> receptors in detrusor smooth muscle
- Multiple products, available as oral or transdermal formulations

**Beta-3 adrenergic agonists**

- Activate beta-3 receptors in detrusor smooth muscle
- Two products, both oral

1. Brucker BM et al. Urology. 2020;145:52-59. 2. Gormley EA et al. J Urol. 2012;188(6 suppl):2455-2463. 3. Andersson KE. Eur Urol. 2011;59:377-386. 4. Chapple CR. Eur Urol. 2012;82:341-343. 5. Lightner DJ et al. J Urol. 2015;202:558-569. PeerView.com

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# Considering Safety and Efficacy in Antimuscarinics

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### Multiple Choices, Longstanding Use<sup>1</sup>

- AUA/SUFU rate all as comparable in efficacy: darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium
- Antimuscarinics bind to receptors in multiple sites, resulting in off-target AEs that include dry mouth, constipation, dry eyes, blurred vision, dyspepsia, UTI, urinary retention, impaired cognitive function, and tachycardia
  - Extended-release or transdermal formulations might be associated with less dry mouth

1. Gormley EA et al. J Urol. 2012;188(suppl 6):2455-2463. PeerView.com

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### High Discontinuation Rates<sup>1,2</sup>

- Discontinuation rates are high due to modest efficacy plus AE burden
- In one study of patients ≥66 years of age, 72% stopped treatment within the first year
- In a nursing home population, 67% discontinued treatment before discharge

**Kaplan–Meier Curve: Discontinuation Probability by Type of Antimuscarinic Medication in a Cohort of Nursing Home Residents (N = 11,012)**

1. Aparasu RR et al. Adv Ther. 2020;37:3584-3605. 2. Vouri SM et al. Arch Gerontol Geriatr. 2019;80:1-11. PeerView.com

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### Limitations of Antimuscarinics<sup>1-6</sup>

- Use with caution in patients with gastric retention, untreated narrow angle glaucoma, and supraventricular tachycardia
- Additive AEs when used with other medications with anticholinergic effects (eg, first-generation H1 antihistamines, muscle relaxants, tricyclic antidepressants, antipsychotics, inhaled anticholinergic bronchodilators)
- Per American Geriatric Society Beers Criteria: “Cumulative exposure to anticholinergic drugs is associated with an increased risk of falls, delirium, and dementia, even in younger adults. Consider total anticholinergic burden.”

1. 2023 American Geriatrics Society Beers Criteria Update Expert Panel. *J Am Geriatrics Soc*. 2023;71(7):2052-2081.  
 2. Gray SL et al. *JAMA*. 2015;313(17):461. 3. Campbell NL et al. *Pharmacotherapy*. 2018;38(5):511-519. 4. Fox C et al. *Age Ageing*. 2014;43:604-615.  
 5. Szabo SM et al. *BMJ Open*. 2019;9:e026391. 6. Chatterjee S et al. *Expert Opin Drug Saf*. 2020;19(12):1-1267.

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### Anticholinergic Burden Is Associated With Elevated Risk for Cognitive Impairment<sup>1-6</sup>

- Multiple studies have found evidence that anticholinergic burden is associated with elevated risk for cognitive impairment among patients with OAB
- Yet a recent article is titled “Despite Recommendations, Anticholinergics Account for the Majority of Prescriptions to Treat Overactive Bladder in the United States”
  - 2013-2019: Medicare Part D beneficiaries ≥65 years of age received 47.7 million 30-day prescriptions for OAB
  - In 2013, anticholinergics represented 98% of 30-day prescriptions
  - In 2019, anticholinergics still comprised the majority of prescriptions in this cohort—although the use of beta-3 agonists was nearly 24 times greater than in 2013

1. Gray SL et al. *JAMA*. 2015;313(17):461. 2. Campbell NL et al. *Pharmacotherapy*. 2018;38(5):511-519. 3. Fox C et al. *Age Ageing*. 2014;43:604-615.  
 4. Szabo SM et al. *BMJ Open*. 2019;9:e026391. 5. Chatterjee S et al. *Expert Opin Drug Saf*. 2020;19(12):1-1267. 6. Carr DN et al. *Urology*. 2023;29:497-503.

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## Considering Safety and Efficacy in Beta-3 Adrenergic Agonists

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**Mirabegron, FDA Approved in 2012<sup>1-6</sup>**

- Safety, efficacy, and tolerability demonstrated in phase 3 and 4 trials including SYNERGY I/II, BESIDE, PILLAR
  - Decreased urinary frequency and UI, with statistically significant and clinically meaningful improvements in QOL scores
- Administration: 25 mg and 50 mg tablets, QD
- Associated with elevations in BP; periodic BP checks advised
- Should not be used by patients with severe, uncontrolled HTN
- CYP2D6 inhibitor
- Most common AEs: HTN, nasopharyngitis, UTI, headache

1. Inoue M et al. *Acta Med Okayama*. 2019;73:387-392. 2. Herdman M et al. *Patent*. 2017;10:677-686. 3. Gratzke C et al. *Eur Urol*. 2016;74:501-509. 4. Wagg A et al. *Eur Urol*. 2020;77:211-220. 5. Chapple CR et al. *Eur Urol*. 2020;77:119-128. 6. Mybentziq [mirabegron] Prescribing Information. [https://www.accessdata.fda.gov/drugsatfd\\_docs/label/2021/20200110mg/1s0175a.pdf](https://www.accessdata.fda.gov/drugsatfd_docs/label/2021/20200110mg/1s0175a.pdf). PeerView.com

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**Predicting Mirabegron Treatment Response: A Post Hoc Analysis From Clinical Trials<sup>1</sup>**

- Given high discontinuation rates associated with some OAB medications, researchers sought to identify a model for predicting individual treatment response to mirabegron to guide prescribing decisions and set realistic patient expectations to support adherence/persistence
- Better response in patients with  $\geq 3$  urgency episodes at baseline, mixed stress and UUI, and  $>5$  urgency episodes/d
- Lower response associated with prior use of  $\geq 3$  OAB medications, BMI  $\geq 30$  kg/m<sup>2</sup>, OAB symptom duration  $\geq 12$  months, baseline incontinence, concomitant use of BPH medication

1. Matta R et al. *Eur Urol Focus*. 2023;27:S2406-4569(23)00100-1. PeerView.com

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**Vibegron, FDA Approved in 2020<sup>1-6</sup>**

- Safety, efficacy, and tolerability demonstrated in phase 3 EMPOWUR trial and extension studies
  - Significant improvements in urinary frequency, urgency, and UUI episodes; demonstrated superiority to tolterodine in UUI
  - Patient-reported improvements in QOL, sleep, symptom bother
- Administration: 75 mg tablet, QD
- Does not cross blood–brain barrier; is not associated with cognitive AEs
- Does not induce or inhibit CYP2D6 and CYP3A4 enzyme activity, so drug–drug interactions are limited
- Most common AEs: headache, UTI, nasopharyngitis, diarrhea, nausea, URTI

1. Varano S et al. *Drugs Aging*. 2021;38:137-146. 2. Edmondson SD et al. *J Med Chem*. 2016;59:609-623. 3. Staskin D et al. *Urol*. 2021;205:1421-1429. 4. Reithberger F. *Expert Opin Pharmacother*. 2021;22:3-17. 5. Gemtesa [vibegron] Prescribing Information. [https://www.accessdata.fda.gov/drugsatfd\\_docs/label/2020/2020011300560020a.pdf](https://www.accessdata.fda.gov/drugsatfd_docs/label/2020/2020011300560020a.pdf). 6. Frankel J et al. *Int J Clin Pract*. 2021;75:e13937. PeerView.com

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### Phase 4 Trial: Looking for Real-World Data on Vibegron<sup>1</sup>

- Recruitment is ongoing for Composur, an open-label prospective study to assess patient treatment satisfaction, QOL, and healthcare resource utilization
- Participants previously treated with anticholinergics, mirabegron, or combination therapy (eg, mirabegron + solifenacin) will be treated with vibegron
- Primary endpoints: mean satisfaction domain score assessed by OAB-SATq score at 3, 6, and 12 months
- Secondary endpoints: responses to individual satisfaction scores, additional OAB-SATq domain scores, and safety
- **Exploratory endpoints are adherence and persistence**
- Estimated study completion date: September 2024

1. Dmochowski RR et al. BMC Urol. 2023;23:64.

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### Cardiovascular Considerations in OAB Management<sup>1-3</sup>

- Prevalence of CV comorbidities, including HTN, is higher in patients with OAB than in patients without OAB
- Anticholinergics are associated with QT prolongation and elevated HR
- Beta-3 adrenergic receptors, expressed on detrusor smooth muscle, are also expressed in cardiac tissue, raising concerns for off-target CV effects
  - Mirabegron is associated with elevations in HR
  - In the EMPOWUR trial, vibegron demonstrated hypertension rates similar to placebo

1. Chapple CR et al. Int Urogynecol J. 2013;24:1447-1458. 2. Nils VW et al. Int J Clin Pract. 2014;68:972-985. 3. Weber MA et al. Blood Press Monit. 2022;27:128-134.

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### Randomized Controlled Trial: Ambulatory BP in Vibegron Users<sup>1</sup>

- Patients with OAB (N = 214) randomized to vibegron 75 mg/d or placebo
  - 39.6% of the treatment group and 30.7% of the placebo group had pre-existing HTN
- Primary endpoint: change from baseline in mean daytime ambulatory systolic BP
- Secondary endpoints: change from baseline in mean 24-hr systolic BP, mean daytime and mean 24-hr diastolic BP, and HR
- Conclusion: No statistically significant or clinically relevant effect on BP or HR in vibegron vs placebo, regardless of baseline HTN status

1. Weber MA et al. Blood Press Monit. 2022;27:128-134.

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### Comparing Beta-3 Adrenoreceptor Agonists: Recent Head-to-Head Data<sup>1</sup>

- A prospective randomized crossover study in 80 OAB treatment-naïve women ≥50 years of age compared the efficacy and safety of mirabegron and vibegron
- 39 patients used mirabegron 50 mg/d for 8 weeks followed by vibegron 50 mg/d for 8 weeks (no washout period); 41 patients used the drugs in the opposite order
- Assessments at baseline, week 8, and week 16 were Overactive Bladder Symptom Score (day/night frequency, urgency, UUI) and frequency volume chart
- Results: Efficacy and safety parameters were similar. Asked about their preferences, 26% of patients chose mirabegron, 58% of patients chose vibegron, and 16% had no preference

1. Wada N et al. Urology. 2023;209:1184.

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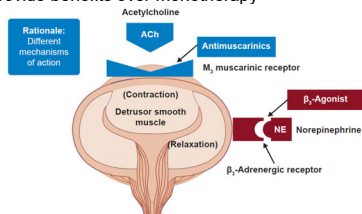
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### Another Direction in OAB Management: Combination Therapy

- Behavioral therapy plus drug therapy yields additive value
- Combining medications that leverage different mechanisms of action might also provide benefits over monotherapy



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### 2019 AUA/SUFU OAB Guideline Update Includes Combination Drug Therapy for OAB<sup>1-4</sup>

- “Clinicians may consider combination therapy with an antimuscarinic and beta-3-adrenoceptor agonist for patients refractory to monotherapy with either”
- Trial evidence supports improved efficacy of certain drug combinations over monotherapy with either drug, with no significant safety effects
  - SYNERGY I and II: solifenacin + mirabegron, solifenacin or mirabegron, placebo
  - BESIDE: solifenacin + mirabegron, solifenacin monotherapy
- The authors called for further research to evaluate combination therapy with other drug classes and dosing regimens

1. Lighner DJ et al. J Urol. 2019;202:558-563. 2. Herschorn S et al. BJU Int. 2017;120:562-575. 3. Gratzke C et al. Eur Urol. 2018;74:501. 4. Drake MG et al. Eur Urol. 2016;70:136.

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### Is Gene Therapy on the OAB Horizon?<sup>1</sup>

- Safety and efficacy findings from a phase 2A randomized, double-blind, placebo-controlled trial of investigative gene therapy URO-902 were presented at the 2023 AUA meeting
- URO-902 was administered by intradetrusor injection by cystoscopy under local anesthesia
- Both 24 mg and 48 mg doses were associated with reductions from baseline of daily micturitions, urgency episodes, and UUI episodes starting at week 2 and persisting through 48 weeks
- Most common AEs were UTI and hematuria

1. Peters KM et al. Urology. 2023;209:e1194.

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### Summary and Take-Home Messages

- OAB is a syndrome with urinary urgency as the core symptom
  - Daytime frequency, nocturia, and urge incontinence might also be present
- Both men and women are affected, although OAB symptoms in men are frequently mistaken for BPH
- Initial assessment of uncomplicated patients requires only a focused history plus physical exam and urinalysis
- OAB becomes more prevalent with advancing age and accumulated comorbidities, and polypharmacy concerns affect treatment decisions
- Beta-3 adrenergic receptor agonists, the newest class of OAB medications, have demonstrated efficacy without some of the drawbacks associated with antimuscarinics (eg, dry mouth, constipation, elevated risk of falls, negative effects on cognition)
  - There are clinically relevant distinctions between the two agents in the class
- Effective management of OAB in LTC holds the potential to improve patient outcomes and reduce the risks and burdens associated with incontinence for patients, staff, and the facility

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## Audience Q&A



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Please remember to complete and submit your Post-Test and Evaluation for CE credit.

[PeerView.com/OveractiveBladder-Survey-QGG](https://PeerView.com/OveractiveBladder-Survey-QGG)



Thank you and have a good day.

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### Abbreviations

- Ach: acetylcholine
- AUA: American Urological Association
- $\beta_3$ : beta 3
- B-SAQ: Bladder Control Self-Assessment Questionnaire
- CMS: Centers for Medicare and Medicaid Services
- CNA: certified nursing assistant
- CYP2D6: cytochrome P450 family 2 subfamily D member 6
- CYP3A4: cytochrome P450 family 3 subfamily A member 4
- DON: director of nursing
- EOT: end of treatment
- H1: first generation histamine
- HR: heart rate
- HTN: hypertension
- ICS: Incident Command System
- LTC: long-term care
- LUTS: lower urinary tract symptoms
- $M_2$ : muscarinic receptor 2
- $M_3$ : muscarinic receptor 3
- NE: norepinephrine
- NPH: normal pressure hydrocephalus
- OAB: overactive bladder
- OAB-SATq: Overactive Bladder Satisfaction With Treatment Questionnaire
- OAB-V3: Overactive Bladder Awareness Tool—3-item
- OAB-V8: Overactive Bladder-Validated 8-question Screener
- QD: once daily
- SUFU: Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
- T2DM: type 2 diabetes mellitus
- TEAE: treatment-emergent adverse event
- UI: urinary incontinence
- UIL: urinary interleukin
- URTI: upper respiratory tract infection
- UUI: urge urinary incontinence

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