# NEW DRUG APPROVAL

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| **Brand Name** | Gemtesa® |
| **Generic Name** | vibegron |
| **Drug Manufacturer** | Urovant Sciences, Inc. |

## New Drug Approval

FDA Approval Date: December 23, 2020

Review Designation: Standard

Type of Review: Type 1 – New Molecular Entity

Dispensing Restrictions: N/A

## Place in Therapy

### DISEASE DESCRIPTION & EPIDEMIOLOGY

Overactive bladder (OAB) is a condition in which the bladder squeezes urine out at the wrong time. You may have overactive bladder if you have two or more of these symptoms:

- You urinate eight or more times a day or two or more times at night.
- You have the sudden, strong need to urinate immediately.
- You leak urine after a sudden, strong urge to urinate.

Urinary incontinence, the involuntary leakage of urine, is often underdiagnosed and undertreated. In one survey, only 60 percent of patients seeking care for leakage that occurred at least once weekly recalled receiving any treatment for their incontinence. Additionally, nearly 50 percent of those who did receive treatment reported moderate to great frustration with ongoing incontinence.

In the National Overactive Bladder Evaluation (NOBLE) study, which evaluated 5204 adults 18 years of age and older who were representative of the US population by sex, age, and geographical region, 16.5% of the study participants met the criteria for OAB. Of those, 6.1% met the criteria for OAB with urgency incontinence, and 10.4% met criteria for OAB without urgency incontinence. Among individuals with OAB with urgency incontinence, 45% had mixed incontinence symptoms (urgency incontinence plus stress incontinence). Data in the study were gathered with the use of a computer-assisted telephone interview questionnaire.

## Efficacy

The efficacy of Gemtesa® was evaluated in a 12-week, double-blind, randomized, placebo-controlled, and active-controlled trial (Study 3003, NCT03492281) in patients with OAB (urge urinary incontinence, urgency, and urinary frequency). Patients were randomized 5:5:4 to receive either Gemtesa® 75 mg, placebo, or active control orally, once daily for 12 weeks. For study entry, patients had to have symptoms of OAB for at least 3 months with an average of 8 or more micturitions per day and at least 1 urge urinary incontinence (UUI) per day, or an average of 8 or more micturitions per day and an average of at least 3 urgency episodes per day. Urge urinary incontinence was defined as leakage of urine of any amount because the patient felt an urge or need to urinate immediately. The study population included OAB medication-naïve patients as well as patients who had received prior therapy with OAB medications. The co-primary endpoints were change from baseline in average daily number of micturitions and average daily number of UUI episodes at week 12. Additional endpoints included change from baseline in average daily number of "need to urinate immediately" (urgency) episodes and average volume voided per micturition. A total of 1,515 patients received at least one daily dose of placebo (n=540), Gemtesa® 75 mg

(n=545), or an active control treatment (n=430). The majority of patients were Caucasian (78%) and female (85%) with a mean age of 60 (range 18 to 93) years. reviews of randomized trials have found that antimuscarinics have a modest benefit over placebo in reducing urgency incontinence. Cure rates for anticholinergic medications are low (49 percent, interquartile range [IQR] 35.6-58%). The efficacy of all the antimuscarinic agents is thought to be similar.

A systematic review including 72 randomized trials found that antimuscarinic medications were more effective than placebo at improving urinary incontinence, but with low magnitude of effect. A dose response for efficacy or adverse effect was inconsistently observed. Conclusions regarding comparative effectiveness and safety of the antimuscarinic agents are precluded by the paucity of head-to-head trials between specific agents.

Gemtesa® was also evaluated for long-term safety in an extension study (Study 3004) in 505 patients who completed the 12-week study (Study 3003). Of the 273 patients who received Gemtesa® 75 mg once daily in the extension study, 181 patients were treated for a total of one year.

**Mean Baseline and Change from Baseline at Week 12 for Micturition Frequency, Urge Urinary Incontinence Episodes, "Need to Urinate Immediately" (Urgency) Episodes, and Volume Voided per Micturition.**

| Parameter | GEMTESA 75 mg | Placebo |
|---|---|---|
| **Average Daily Number of Micturitions** | | |
| Baseline mean (n) | 11.3 (526) | 11.8 (520) |
| Change from Baseline▪ (n) | -1.8 (492) | -1.3 (475) |
| Difference from Placebo | -0.5 | |
| 95% Confidence Interval | -0.8, -0.2 | |
| p-value | <0.001 | |
| **Average Daily Number of UUI Episodes** | | |
| Baseline mean (n) | 3.4 (403) | 3.5 (405) |
| Change from Baseline▪ (n) | -2.0 (383) | -1.4 (372) |
| Difference from Placebo | -0.6 | |
| 95% Confidence Interval | -0.9, -0.3 | |
| p-value | <0.0001 | |
| **Average Daily Number of "Need to Urinate Immediately" (Urgency) Episodes** | | |
| Baseline mean (n) | 8.1 (526) | 8.1 (520) |
| Change from Baseline▪ (n) | -2.7 (492) | -2.0 (475) |
| Difference from Placebo | -0.7 | |
| 95% Confidence Interval | -1.1, -0.2 | |
| p-value | 0.002 | |
| **Average Volume Voided (mL) per Micturition** | | |
| Baseline mean (n) | 155 (524) | 148 (514) |
| Change from Baseline▪ (n) | 23 (490) | 2 (478) |
| Difference from Placebo | 21 | |
| 95% Confidence Interval | 14, 28 | |
| p-value | <0.0001 | |
| ▪ Least squares mean adjusted for treatment, baseline, sex, geographical region, study visit, and study visit by treatment interaction term. | | |

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## Safety

### ADVERSE EVENTS

Most common adverse reactions (≥2%) reported with Gemtesa® were headache, urinary tract infection, nasopharyngitis, diarrhea, nausea, and upper respiratory tract infection.

### WARNINGS & PRECAUTIONS

Urinary Retention: Monitor for urinary retention, especially in patients with bladder outlet obstruction and also in patients taking muscarinic antagonist medications for OAB, in whom the risk of urinary retention may be greater. If urinary retention develops, discontinue Gemtesa®.

### CONTRAINDICATIONS

Do not use if prior hypersensitivity reaction to vibegron or any components of the product.

## Clinical Pharmacology

### MECHANISMS OF ACTION

Vibegron is a selective human beta-3 adrenergic receptor agonist. Activation of the beta-3 adrenergic receptor increases bladder capacity by relaxing the detrusor smooth muscle during bladder filling.

## Dose & Administration

### ADULTS

The recommended dose is one 75 mg tablet once daily.

### PEDIATRICS

The safety and effectiveness of Gemtesa® in pediatric patients has not been established.

### GERIATRICS

Refer to adult dosing.

### RENAL IMPAIRMENT

eGFR 15 mL/minute/1.73 $m^2$ or more: No dosage adjustment is needed.

eGFR 0 to 14 mL/minute/1.73 $m^2$ (with or without hemodialysis): Use not recommended; vibegron has not been studied in this population.

### HEPATIC IMPAIRMENT

Mild to moderate hepatic impairment (Child-Pugh A and B): No dosage adjustment is needed.

Severe hepatic impairment (Child-Pugh C): Use is not recommended; vibegron has not been studied in this population.

## Product Availability

### DOSAGE FORM(S) & STRENGTH(S)

Tablets: 75 mg