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Vibegron *(Gemtesa)* for Overactive Bladder

The FDA has approved the selective beta-3 adrenergic agonist vibegron (*Gemtesa* – Urovant Sciences) for treatment of overactive bladder in adults with symptoms of urge urinary incontinence, urgency, and urinary frequency. It is the second beta-3 agonist to be approved in the US; mirabegron *(Myrbetriq)* was the first.[1]

Pronunciation Key

Vibegron: vye beg' ron **Gemtesa:** jem tes' ah

STANDARD TREATMENT — Overactive bladder (OAB) causes urgency, frequency, nocturia, and incontinence. It occurs most commonly in older women. Management with behavioral modification, including bladder training, urge suppression, pelvic floor muscle exercises, and avoidance of dietary irritants such as alcohol and caffeine, should be tried first.

Anticholinergic drugs, such as tolterodine (*Detrol*, and generics) and solifenacin (*Vesicare*, and generics), reduce OAB symptoms by inhibiting involuntary bladder contractions and relaxing detrusor smooth muscle, but they can cause dry mouth and constipa-tion, and their long-term use has been associated with a dose-related increase in the risk of dementia.[2] Mirabegron appears to be similar in effectiveness to anticholinergic drugs and better tolerated, but it has been associated with small increases in blood pressure.[3]

Combination therapy with an anticholinergic drug and a beta-3 agonist can be considered when monotherapy is ineffective; mirabegron is FDA-approved for use both alone and in combination with solifenacin. Options for patients with refractory OAB include peripheral tibial nerve stimulation, sacral neuromodulation, and intra-detrusor injection of onabotulinumtoxinA *(Botox)*.[1,4]

Summary: Vibegron *(Gemtesa)*

- FDA-approved for treatment of overactive bladder in adults with symptoms of urge urinary incontinence, urgency, and urinary frequency.
- Second beta-3 agonist to be approved for treatment of overactive bladder; mirabegron *(Myrbetriq)* was the first.
- Decreased mean daily micturitions compared to placebo and appeared to be similar in efficacy to the anticholinergic drug tolterodine in a double-blind clinical trial.
- Unlike mirabegron, vibegron has not been associated with blood pressure elevations.
- Taken once daily with a glass of water; tablets can be swallowed whole or crushed and mixed with applesauce.

MECHANISM OF ACTION — Like mirabegron, vibegron activates beta-3 adrenergic receptors in the bladder, resulting in relaxation of detrusor smooth muscle during the storage phase of the fill-void cycle and increased bladder capacity. Although no direct comparisons are available, vibegron appears to be more selective than mirabegron *in vitro* for beta-3 receptors compared to beta-1 and beta-2 receptors.[5,6]

Table 1. Pharmacology

Class	Beta-3 adrenergic agonist
Formulation	75 mg tabs
Route	Oral
Tmax (median)	1-3 hours
Metabolism	CYP3A4 (minor)
Elimination	Feces (59%; 54% as unchanged drug); urine (20%)
Half-life (mean)	30.8 hours

CLINICAL STUDIES — FDA approval of vibegron was based on the results of a 12-week, double-blind trial (EMPOWUR) in 1518 patients with symptomatic OAB who were randomized to receive once-daily treatment with vibegron 75 mg, tolterodine extended-release 4 mg (active control), or placebo. At 12 weeks, the reduction in mean daily micturitions, a coprimary endpoint, was significantly greater with vibegron, but not with tolterodine, compared to placebo (-1.8 with

Table 2. Beta-3 Adrenergic Agonists

	Mirabegron *(Myrbetriq)*	Vibegron *(Gemtesa)*
Formulations	25, 50 mg ER tabs	75 mg tabs
Usual maintenance dosage	25-50 mg once/day	75 mg once/day
Dosage in hepatic impairment	Child-Pugh B: 25 mg once/day Child-Pugh C: not recommended	Child-Pugh C: not recommended
Dosage in renal impairment	eGFR 15-29 mL/min/1.73 m^2: 25 mg once/day eGFR <15 mL/min/1.73 m^2: not recommended	eGFR <15 mL/min/1.73 m^2: not recommended
Administration	Tablets must be swallowed whole and taken with water	Tablets can be swallowed whole or crushed and mixed with apple-sauce; must be taken with water
CYP interactions	Moderate CYP2D6 inhibitor CYP3A4 and 2D6 substrate (minor)	CYP3A4 substrate (minor)
Effect on blood pressure	Can increase up to 3.5/1.5 mm Hg	No clinically significant effect
Cost[1]	$417.20	$458.40

ER = extended-release

1. Approximate WAC for a 30-day supply at the usual maintenance dosage. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2021. Reprinted with permission by First Databank, Inc. All rights reserved. ©2021. www.fdbhealth.com/policies/drug-pricing-policy.

vibegron, -1.6 with tolterodine, and -1.3 with placebo). The reduction in mean daily urge urinary incontinence episodes, the other coprimary endpoint, was significantly greater with both vibegron and tolterodine than with placebo (-2.0 and -1.8 vs -1.4). Patients taking vibegron also had significant improvements, compared to those taking placebo, in volume voided per micturition, urgency episode frequency, and quality of life.[7-9]

ADVERSE EFFECTS — The most common adverse effects that occurred more frequently with vibegron than with placebo in EMPOWUR were headache (4.0% vs 2.4%) and nasopharyngitis (2.8% vs 1.7%). The incidence of hypertension was 1.7% in patients taking vibegron, 1.7% in the placebo group, and 2.6% in the tolterodine group. Urinary retention was reported in 0.6% of patients who took vibegron and in 0.4% of those who took placebo.[7]

PREGNANCY AND LACTATION — No data are available on the use of vibegron in pregnant or lactating women. No adverse effects were observed in the offspring of pregnant animals exposed to 89 times the level of vibegron recommended in humans. Radioactivity has been detected in the milk of lactating rats administered radiolabeled vibegron.

DRUG INTERACTIONS — Taking vibegron with an anticholinergic drug could increase the risk of urinary retention. Concomitant use of vibegron increased the Cmax and AUC of digoxin by 21% and 11%, respectively.

DOSAGE AND ADMINISTRATION — The recommended dosage of vibegron is 75 mg taken orally once daily with a glass of water. The tablets should either be swallowed whole or crushed and mixed with a tablespoonful of applesauce, and consumed immediately. Vibegron is not recommended for use in patients with end-stage renal disease (eGFR <15 mL/min/1.73 m^2) or in those with severe hepatic impairment (Child-Pugh C).

CONCLUSION — The selective beta-3 adrenergic agonist vibegron *(Gemtesa)* was more effective than placebo and appeared to be similar in efficacy to the anticholinergic drug tolterodine for treatment of overactive bladder (OAB) in one 12-week trial. Unlike mirabegron *(Myrbetriq)*, the other beta-3 agonist approved for treatment of OAB, vibegron has not been shown to increase blood pressure, but no direct comparisons of the two drugs are available. Behavioral modification is still preferred for initial treatment of OAB, but mirabegron and vibegron, which have few drug interactions and lack anticholinergic adverse effects, are reasonable choices for patients who require pharmacologic treatment. ■

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