

GEMTESA - vibegron tablet, film coated
Sumitomo Pharma America, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GEMTESA® safely and effectively. See full prescribing information for GEMTESA.

GEMTESA (vibegron) tablets, for oral use
Initial U.S. Approval: 2020

-----**RECENT MAJOR CHANGES**-----

Indications and Usage, Overactive Bladder in Adult Males with Benign Prostatic Hyperplasia (1.2)	12/2024
Contraindications (4)	10/2024
Warnings and Precautions, Angioedema (5.2)	10/2024

-----**INDICATIONS AND USAGE**-----

GEMTESA is a beta-3 adrenergic agonist indicated for the treatment of:

- overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults. (1.1)
- overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adult males on pharmacological therapy for benign prostatic hyperplasia (BPH). (1.2)

-----**DOSAGE AND ADMINISTRATION**-----

- The recommended dose is one 75 mg tablet orally once daily. (2.1)
- Swallow tablet whole with water. (2.1)
- Tablet may be crushed and mixed with applesauce. (2.1)

-----**DOSAGE FORMS AND STRENGTHS**-----

Tablets: 75 mg (3)

-----**CONTRAINDICATIONS**-----

Do not use if prior hypersensitivity reaction to vibegron or any components of the product. (4)

-----**WARNINGS AND 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. (5.1)

Angioedema: Angioedema of the face and/or larynx has been reported with GEMTESA. (5.2)

-----**ADVERSE REACTIONS**-----

Most common adverse reactions ($\geq 2\%$) reported with GEMTESA were headache, urinary tract infection, nasopharyngitis, diarrhea, nausea, and upper respiratory tract infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sumitomo Pharma America, Inc. at 1-833-876-8268 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

Digoxin: Measure serum digoxin concentrations before initiating GEMTESA. Monitor serum digoxin concentrations to titrate digoxin dose to desired clinical effect. (7)

-----**USE IN SPECIFIC POPULATIONS**-----

Pediatric use: Safety and effectiveness in pediatric patients have not been established. (8.4)

End-stage Renal Disease with or without Hemodialysis: Not recommended. (8.6)

Severe Hepatic Impairment: Not recommended. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 2/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

- 1.1 Overactive Bladder in Adults
- 1.2 Overactive Bladder in Adult Males with Benign Prostatic Hyperplasia (BPH)

2 DOSAGE AND ADMINISTRATION

- 2.1 Recommended Dosage

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Urinary Retention
- 5.2 Angioedema

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

- 14.1 Overactive Bladder in Adults
- 14.2 Overactive Bladder in Adult Males with BPH

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Overactive Bladder in Adults

GEMTESA[®] is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults.

1.2 Overactive Bladder in Adult Males with Benign Prostatic Hyperplasia (BPH)

GEMTESA is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adult males on pharmacological therapy for benign prostatic hyperplasia (BPH).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of GEMTESA is one 75 mg tablet orally, once daily with or without food. Swallow GEMTESA tablets whole with a glass of water.

In adults, GEMTESA tablets also may be crushed, mixed with a tablespoon (approximately 15 mL) of applesauce and taken immediately with a glass of water [see *Clinical Pharmacology (12.3)*].

3 DOSAGE FORMS AND STRENGTHS

Tablets: 75 mg, oval, light green, film-coated, debossed with V75 on one side and no debossing on the other side.

4 CONTRAINDICATIONS

GEMTESA is contraindicated in patients with known hypersensitivity to vibegron or any components of GEMTESA. Hypersensitivity reactions, such as angioedema, have occurred [see *Warnings and Precautions (5.2)* and *Adverse Reactions (6.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Urinary Retention

Urinary retention has been reported in patients taking GEMTESA. The risk of urinary retention may be increased in patients with bladder outlet obstruction and also in patients taking muscarinic antagonist medications for the treatment of OAB. Monitor patients for signs and symptoms of urinary retention, particularly in patients with bladder outlet obstruction or patients taking muscarinic antagonist medications for the treatment of OAB. Discontinue GEMTESA in patients who develop urinary retention [see *Adverse Reactions (6.1)*].

5.2 Angioedema

Angioedema of the face and/or larynx has been reported with GEMTESA. Angioedema has been reported to occur hours after the first dose or after multiple doses. Angioedema, associated with upper airway swelling, may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, immediately discontinue GEMTESA and provide appropriate therapy and/or measures necessary to ensure a patent airway. GEMTESA is contraindicated in patients with known hypersensitivity to vibegron or any component of GEMTESA [see *Contraindications (4)* and *Adverse*

[Reactions (6.2)].

6 ADVERSE REACTIONS

The following clinically significant adverse reaction is described elsewhere in the labeling:

- Urinary retention [see *Warnings and Precautions (5.1)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Overactive Bladder in Adults

The safety of GEMTESA was evaluated in a 12-week, double-blind, placebo- and active-controlled study (Study 3003) in patients with OAB [see *Clinical Studies (14.1)*]. A total of 545 patients received GEMTESA. The majority of the patients were White (78%) and female (85%) with a mean age of 60 years (range 18 to 93 years).

Adverse reactions that were reported in Study 3003 at an incidence greater than placebo and in $\geq 2\%$ of patients treated with GEMTESA are listed in Table 1.

Table 1: Adverse Reactions, Exceeding Placebo Rate, Reported in $\geq 2\%$ of Patients Treated with GEMTESA 75 mg for up to 12 Weeks in Study 3003

	GEMTESA 75 mg n (%)	Placebo n (%)
Number of Patients	545	540
Headache	22 (4.0)	13 (2.4)
Nasopharyngitis	15 (2.8)	9 (1.7)
Diarrhea	12 (2.2)	6 (1.1)
Nausea	12 (2.2)	6 (1.1)
Upper respiratory tract infection	11 (2.0)	4 (0.7)

Other adverse reactions reported in $< 2\%$ of patients treated with GEMTESA included:

Gastrointestinal disorders: dry mouth, constipation

Investigations: residual urine volume increased

Renal and urinary disorders: urinary retention

Vascular disorders: hot flush

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.

Adverse reactions reported in $\geq 2\%$ of patients treated with GEMTESA 75 mg for up to 52 weeks in the long-term extension study, and not already listed above, were urinary

tract infection (6.6%) and bronchitis (2.9%).

Overactive Bladder in Adult Males with BPH

The safety of GEMTESA was evaluated in a 24-week double-blind, randomized, placebo-controlled study (Study 3005) in male patients with OAB on pharmacological therapy for BPH. A total of 553 patients received GEMTESA [see *Clinical Studies (14.2)*].

Adverse reactions that were reported in Study 3005 at an incidence greater than placebo and in $\geq 2\%$ of patients treated with GEMTESA are listed in Table 2.

Table 2: Adverse Reactions, Exceeding Placebo Rate, Reported in $\geq 2\%$ of Patients Treated with GEMTESA 75 mg for up to 24 Weeks in Study 3005

	GEMTESA 75 mg n (%)	Placebo n (%)
Number of Patients	553	551
Hypertension*	50 (9.0)	46 (8.3)
Urinary tract infection	14 (2.5)	12 (2.2)

*Defined as an average systolic blood pressure (SBP) ≥ 140 mmHg or diastolic BP (DBP) ≥ 90 mmHg on 3 assessments at two consecutive visits, in non-hypertensive patients.

*Defined as an average increase of SBP ≥ 20 mmHg or DBP ≥ 10 mmHg on 3 assessments at two consecutive visits, or the initiation or increase in dose of antihypertensive medications at any visit, in hypertensive patients.

GEMTESA was also evaluated for long-term safety in a 28-week extension study (Study 3006) in 276 patients who completed the 24-week study (Study 3005). Of the 276 patients who received GEMTESA 75 mg once daily in the extension study, 124 patients were treated for a total of one year.

There were no additional adverse reactions reported in Study 3006 that are not already included in Section 6.1 above.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of vibegron. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse events have been reported in association with vibegron use in worldwide postmarketing experience:

Urologic disorders: urinary retention

Skin and subcutaneous tissue disorders: angioedema of the face and larynx; hypersensitivity reactions, including urticaria, pruritus, rash and drug eruption; eczema

Gastrointestinal disorders: constipation

7 DRUG INTERACTIONS

Concomitant use of GEMTESA increases digoxin maximal concentrations (C_{max}) and systemic exposure as assessed by area under the concentration-time curve (AUC) [see *Clinical Pharmacology (12.3)*]. Serum digoxin concentrations should be monitored before

initiating and during therapy with GEMTESA and used for titration of the digoxin dose to obtain the desired clinical effect. Continue monitoring digoxin concentrations upon discontinuation of GEMTESA and adjust digoxin dose as needed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on GEMTESA use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

In animal studies, no effects on embryo-fetal development were observed following administration of vibegron during the period of organogenesis at exposures approximately 275-fold and 285-fold greater than clinical exposure at the recommended daily dose of GEMTESA, in rats and rabbits, respectively. Delayed fetal skeletal ossification was observed in rabbits at approximately 898-fold clinical exposure, in the presence of maternal toxicity. In rats treated with vibegron during pregnancy and lactation, no effects on offspring were observed at 89-fold clinical exposure. Developmental toxicity was observed in offspring at approximately 458-fold clinical exposure, in the presence of maternal toxicity. No effects on offspring were observed at 89-fold clinical exposure (*see Data*).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies carry some risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In an embryo-fetal developmental toxicity study, pregnant rats were treated with daily oral doses of 0, 30, 100, 300, or 1000 mg/kg/day vibegron during the period of organogenesis (Days 6 to 20 of gestation). These doses were associated with systemic exposures (AUC) 0-, 9-, 89-, 275-, and 1867-fold higher, respectively, than in humans treated with the recommended daily dose of GEMTESA. No embryo-fetal developmental toxicity was observed at doses up to 300 mg/kg/day. Treatment with the high dose of 1000 mg/kg/day was discontinued due to maternal toxicity.

In an embryo-fetal developmental toxicity study, pregnant rabbits were treated with daily oral doses of 0, 30, 100, or 300 mg/kg/day vibegron during the period of organogenesis (Days 7 to 20 of gestation). These doses were associated with systemic exposures (AUC) 0-, 86-, 285-, and 898-fold higher, respectively, than in humans treated with the recommended daily dose of GEMTESA. No embryo-fetal developmental toxicity was observed at doses of vibegron up to 100 mg/kg/day. Maternal toxicity (decreased food consumption), reduced fetal body weight, and an increased incidence of delayed skeletal ossification, were observed at 300 mg/kg/day.

In a pre- and post-natal developmental toxicity study, pregnant or lactating rats were

treated with daily oral doses of 0, 30, 100, or 500 mg/kg/day vibegron from day 6 of gestation through day 20 of lactation. These doses were associated with estimated systemic exposures (AUC) 0-, 9-, 89-, and 458-fold higher, respectively, than in humans treated with the recommended daily dose of GEMTESA. No developmental toxicity was observed in F1 offspring at doses up to 100 mg/kg/day. Maternal toxicity was observed during lactation (decreased body weight gain) at doses \geq 100 mg/kg/day and during gestation (decreased body weight gain and food consumption) at 500 mg/kg/day. Developmental toxicity was observed in F1 offspring (increased stillborn index, lethality, reduced viability and weaning indices, decreased body weight and body weight gains, low physical development differentiation indices, and effects on sensory function and reflexes) at 500 mg/kg/day.

8.2 Lactation

Risk Summary

There are no data on the presence of vibegron in human milk, the effects of the drug on the breastfed infant, or the effects on milk production. When a single oral dose of radiolabeled vibegron was administered to postnatal nursing rats, radioactivity was observed in milk (*see Data*). When a drug is present in animal milk, it is likely that the drug will be present in human milk.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for GEMTESA and any potential adverse effects on the breastfed infant from GEMTESA or from the underlying maternal condition.

Data

Animal Data

In a lactational transfer study, lactating rats were treated with a single oral dose of 10 mg/kg radiolabeled [^3H] vibegron on postpartum day 10. Levels of radioactivity were determined in milk and plasma collected at 1, 4, 12, and 24 after dosing. The C_{max} of total radioactivity in milk and plasma were observed at 9 and 2 hours after dosing, respectively, with a maximum milk-to-plasma concentration ratio of 2.2 observed at 12 hours after dosing. Vibegron elimination from milk showed a similar trend as that from plasma. The radioactivity concentration in milk at 24 hours after administration was approximately 25% of the C_{max} .

8.4 Pediatric Use

The safety and effectiveness of GEMTESA in pediatric patients have not been established.

8.5 Geriatric Use

Of 526 patients who received GEMTESA in the clinical studies for OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency, 242 (46%) were 65 years of age or older, and 75 (14%) were 75 years of age or older [*see Clinical Studies (14.1)*]. No overall differences in safety or effectiveness of GEMTESA have been observed between patients 65 years of age and older and younger adult patients.

Of the total number of GEMTESA-treated patients in clinical studies for OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency in adult males

on pharmacological therapy for benign prostatic hyperplasia (BPH), 347 (63%) were 65 years of age and older, while 100 (18%) were 75 years of age and older [see *Clinical Studies (14.2)*]. No overall differences in safety of GEMTESA have been observed between patients 65 years of age and older and younger adult patients.

8.6 Renal Impairment

No dosage adjustment for GEMTESA is recommended for patients with mild, moderate, or severe renal impairment (eGFR 15 to <90 mL/min/1.73 m²). GEMTESA has not been studied in patients with eGFR <15 mL/min/1.73 m² (with or without hemodialysis) and is not recommended in these patients [see *Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

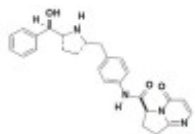
No dosage adjustment for GEMTESA is recommended for patients with mild to moderate hepatic impairment (Child-Pugh A and B). GEMTESA has not been studied in patients with severe hepatic impairment (Child-Pugh C) and is not recommended in this patient population [see *Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

There is no experience with inadvertent GEMTESA overdosage. In case of suspected overdose, treatment should be symptomatic and supportive.

11 DESCRIPTION

Vibegron is a selective beta-3 adrenergic agonist. The chemical name is (6S)-N-[4-[[[(2S,5R)-5-[(R)-hydroxy(phenyl)methyl]pyrrolidin-2-yl]methyl]phenyl]-4-oxo-7,8-dihydro-6H-pyrrolo[1,2-a]pyrimidine-6-carboxamide having a molecular formula of C₂₆H₂₈N₄O₃ and a molecular weight of 444.538 g/mol. The structural formula of vibegron is:



Vibegron is a crystalline, white to off-white to tan powder.

GEMTESA tablets, for oral administration contain 75 mg of vibegron and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, mannitol, and microcrystalline cellulose. The light green film coating contains FD&C Blue No. 2 - aluminum lake, hypromellose, iron oxide yellow, lactose monohydrate, titanium dioxide, and triacetin.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism 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.

12.2 Pharmacodynamics

Vibegron's exposure-response relationship and the time course of pharmacodynamic response are not fully characterized.

Blood Pressure

In a 4-week, randomized, placebo-controlled, ambulatory blood pressure study in OAB patients (n=200), daily treatment with GEMTESA 75 mg was not associated with clinically significant changes in blood pressure. Subjects enrolled in this study had a mean age of 59 years and 75% were female. Thirty-five percent of subjects had pre-existing hypertension at baseline and 29% of all subjects were taking at least 1 concomitant antihypertensive medication.

Cardiac Electrophysiology

GEMTESA does not prolong the QT interval to any clinically relevant extent at a single dose 5.3 times the approved recommended dose.

12.3 Pharmacokinetics

Mean vibegron C_{max} and AUC increased in a greater than dose-proportional manner up to 600 mg (8 times the approved recommended dosage). Steady state concentrations are achieved within 7 days of once daily dosing. The mean accumulation ratio (R_{ac}) was 1.7 for C_{max} and 2.4 for AUC_{0-24hr} .

Absorption

Median vibegron T_{max} is approximately 1 to 3 hours.

Oral administration of a 75 mg vibegron tablet crushed and mixed with 15 mL of applesauce resulted in no clinically relevant changes in vibegron pharmacokinetics when compared to administration of an intact 75 mg vibegron tablet.

Effect of Food

No clinically significant differences in vibegron pharmacokinetics were observed following administration of a high-fat meal (53% fat, 869 calories [32.1 g protein, 70.2 g carbohydrate, and 51.1 g fat]).

Distribution

The mean apparent volume of distribution is 6304 liters. Human plasma protein binding of vibegron is approximately 50%. The average blood-to-plasma concentration ratio is 0.9.

Elimination

Vibegron has an effective half-life of 30.8 hours across all populations.

Metabolism

Metabolism plays a minor role in the elimination of vibegron. CYP3A4 is the predominant enzyme responsible for in vitro metabolism.

Excretion

Following a radiolabeled dose, approximately 59% of the dose (54% as unchanged) was

recovered in feces and 20% (19% as unchanged) in urine.

Specific Populations

No clinically significant differences in the pharmacokinetics of vibegron were observed based on age (18 to 93 years), sex, race/ethnicity (Japanese vs. non-Japanese), mild (eGFR 60 to <90 mL/min/1.73 m²), moderate (eGFR 30 to <60 mL/min/1.73 m²), and severe (eGFR 15 to <30 mL/min/1.73 m²) renal impairment, or moderate (Child-Pugh B) hepatic impairment. The effect of more severe renal impairment (eGFR <15 mL/min/1.73 m²) with or without hemodialysis or severe (Child-Pugh C) hepatic impairment on vibegron pharmacokinetics was not studied.

Drug Interaction Studies

Clinical Studies

Digoxin: Concomitant administration of vibegron increased digoxin C_{max} and AUC by 21% and 11%, respectively.

Other Drugs: No clinically significant differences in vibegron pharmacokinetics were observed when used concomitantly with ketoconazole (P-gp and strong CYP3A4 inhibitor), diltiazem (P-gp and moderate CYP3A4 inhibitor), rifampin (strong CYP3A4 inducer), or tolterodine. No clinically significant differences in the pharmacokinetics of the following drugs were observed when used concomitantly with vibegron: tolterodine, tolterodine 5-hydroxy metabolite, metoprolol, combined oral contraceptive (ethinyl estradiol, levonorgestrel), or warfarin.

In Vitro Studies

Cytochrome P450 (CYP) Enzymes: Vibegron is a CYP3A4 substrate. Vibegron did not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4. Vibegron did not induce CYP1A2, CYP2B6, or CYP3A4.

Transporter Systems: Vibegron is a P-gp substrate. Vibegron did not inhibit P-gp, BCRP, OATP1B1, OATP1B3, OAT1, OAT3, OCT1, OCT2, MATE1, or MATE2K at clinically relevant concentrations.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No carcinogenicity was observed in long-term studies conducted in mice and rats treated with daily oral doses of vibegron for approximately 2 years. In the mouse carcinogenicity study, CD-1 mice were treated with daily oral doses of vibegron up to 90 mg/kg/day in males and up to 150 mg/kg/day in females, corresponding to estimated systemic exposures (AUC) 21- and 55-fold higher, respectively, than in humans treated with the recommended daily dose of GEMTESA. In the rat carcinogenicity study, Sprague Dawley rats were treated with daily oral doses of vibegron up to 30 mg/kg/day in males and up to 180 mg/kg/day in females, corresponding to systemic exposures (AUC) 18- and 117-fold higher, respectively, than in humans treated with the recommended daily dose of GEMTESA.

Mutagenesis

Vibegron was not mutagenic in *in vitro* microbial reverse mutation assays, showed no evidence of genotoxic activity in an *in vitro* human peripheral blood lymphocyte chromosomal aberration assay, and did not increase the frequency of micronucleated polychromatic erythrocytes in an *in vivo* rat bone marrow micronucleus assay.

Impairment of Fertility

In fertility/general reproductive toxicity studies conducted in rats, females were treated with daily oral doses of 0, 30, 100, 300, or 1000 mg/kg/day vibegron and males were treated with daily oral doses of 0, 10, 30, or 300 mg/kg/day vibegron. No effects on fertility were observed in female or male rats at doses up to 300 mg/kg/day, associated with systemic exposure (AUC) at least 274-fold higher than in humans treated with the recommended daily dose of GEMTESA. General toxicity, decreased fecundity, and decreased fertility were observed in female rats at 1000 mg/kg/day, associated with estimated systemic exposure 1867-fold higher than in humans treated with the recommended daily dose of GEMTESA.

14 CLINICAL STUDIES

14.1 Overactive Bladder in Adults

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 White (78%) and female (85%) with a mean age of 60 (range 18 to 93) years.

Table 3 shows changes from baseline at week 12 for average daily number of micturitions, average daily number of UUI episodes, average daily number of “need to urinate immediately” (urgency) episodes, and average volume voided per micturition.

Table 3: 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.

Figure 1 and Figure 2 show the mean change from baseline over time in average daily number of micturitions and mean change from baseline over time in average daily number of UUI episodes, respectively.

Figure 1: Mean (SE) Change from Baseline in the Average Daily Number of Micturitions

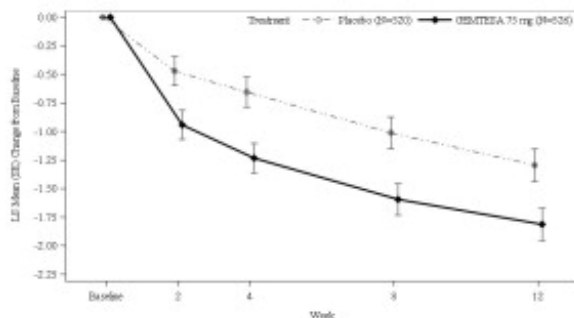
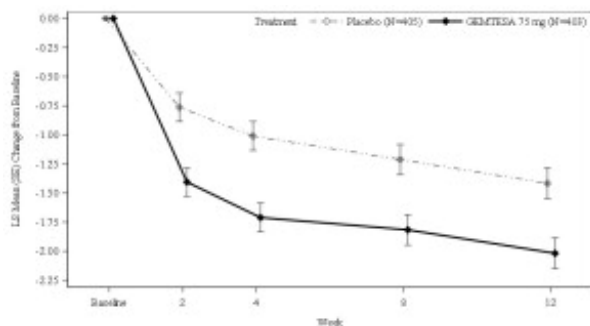


Figure 2: Mean (SE) Change from Baseline in the Average Daily Number of UUI Episodes in Patients with At Least 1 Average Daily UUI Episode at Baseline



14.2 Overactive Bladder in Adult Males with BPH

The safety, tolerability, and efficacy of GEMTESA was evaluated in a multinational 24-week, double-blind, randomized, placebo-controlled trial (Study 3005, NCT03902080) in male patients at least 45 years of age with OAB on pharmacological therapy (i.e., treatment with an alpha blocker, with or without a 5-alpha reductase inhibitor) for BPH. A total of 1105 patients were randomized 1:1 to receive either GEMTESA 75 mg or placebo once daily for 24 weeks. For study entry, patients had symptoms of OAB (an average of 8 or more micturitions per day, 3 or more urgency episodes per day with or without incontinence, and 2 or more nocturia episodes per night) while taking pharmacological therapy for at least 2 months for the treatment of lower urinary tract symptoms due to BPH. Randomization was stratified based on the baseline average number of micturition episodes per day, alpha blocker use with or without 5 alpha reductase inhibitor use, and urinary incontinence.

The co-primary endpoints were change from baseline in the average daily number of micturitions and the average daily number of “need to urinate immediately” (urgency) episodes at week 12. Additional endpoints included change from baseline in the average daily number of urge urinary incontinence (UUI) episodes and the average volume voided per micturition.

A total of 1104 patients received at least one daily dose of placebo (n=551) or GEMTESA 75 mg (n=553). The majority of patients were White (87%) and enrolled in the U.S. (56%). The mean age was 67 years (range 45 to 97) and at least 63% were ≥ 65 years.

Table 4 shows changes from baseline at week 12 for average daily number of micturitions, average daily number of urgency episodes, average daily number of UUI episodes and average volume voided per micturition.

Table 4: Mean Baseline and Change from Baseline at Week 12 for Micturition Frequency, "Need to Urinate Immediately" (Urgency Episodes), UUI Episodes and Volume Voided per Micturition

Parameter	GEMTESA 75 mg (N = 538)	Placebo (N = 542)
Average Daily Number of Micturitions		
Baseline mean	11.84	11.96
Change from Baseline*	-2.04	-1.30
Difference from Placebo	-0.74	
95% Confidence Interval	-1.02, -0.46	

Average Daily Number of “Need to Urinate Immediately” (Urgency) Episodes		
Baseline mean	9.05	9.00
Change from Baseline*	-2.88	-1.93
Difference from Placebo	-0.95	
95% Confidence Interval	-1.37, -0.54	
Average Daily Number of UUI Episodes		
N ***	146	151
Baseline mean	3.33	3.23
Change from Baseline*	-2.19	-1.39
Difference from Placebo	-0.80	
95% Confidence Interval	-1.33, -0.27	
Average Volume Voided (mL) per Micturition		
Baseline mean	166.37	166.43
Change from Baseline*	25.63	10.56
Difference from Placebo	15.07	
95% Confidence Interval	9.13, 21.02	

* Least squares mean adjusted for study visit, baseline value, geographical region, interaction of visit by treatment, and stratification factors as randomized (baseline average micturitions per day**, alpha blocker use with or without 5-ARI, baseline urinary incontinence**), geographical region, study visit, and study visit by treatment interaction term.

** Baseline average micturitions per day stratification factor is not included in the model where the continuous value of baseline average micturitions per day is present; baseline urinary incontinence is not included in the model for UUI;

*** Only subjects with baseline incontinence have UUI analyzed.

Figure 3 and Figure 4 show the mean change from baseline over time in average daily number of micturitions and mean change from baseline over time in average daily number of urgency episodes, respectively.

Figure 3: Mean (SE) Change from Baseline in the Average Daily Number of Micturitions in Male Patients with BPH on Pharmacological Therapy

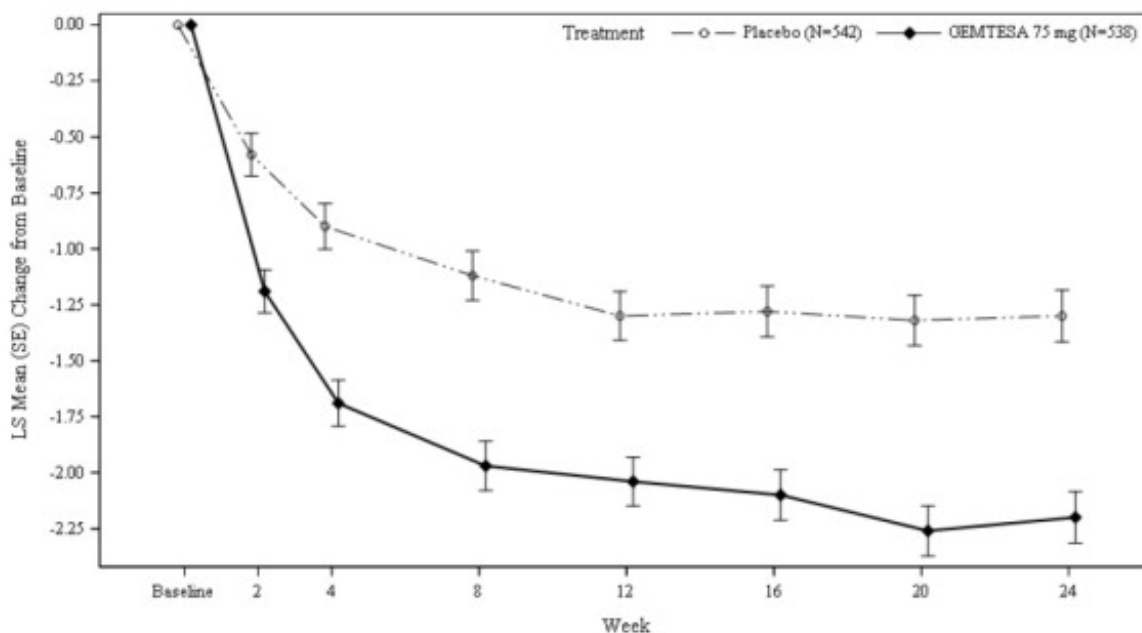
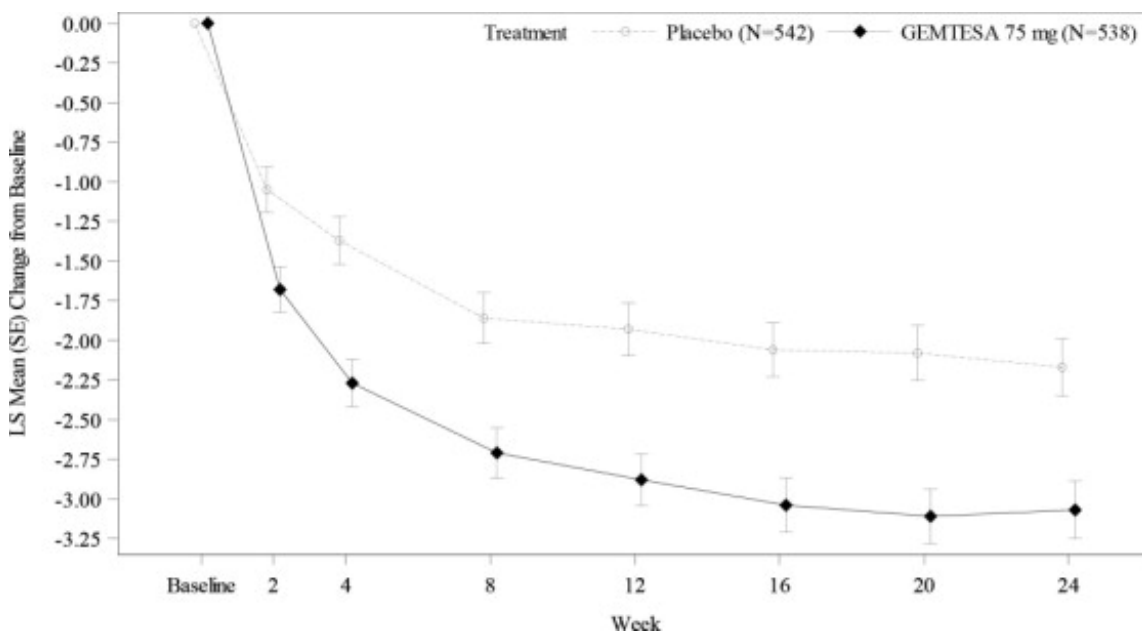


Figure 4: Mean (SE) Change from Baseline in the Average Daily Number of Urgency Episodes in Male Patients with BPH on Pharmacological Therapy



16 HOW SUPPLIED/STORAGE AND HANDLING

GEMTESA 75 mg tablets are light green, oval, film-coated tablets, debossed with V75 on one side and no debossing on the other side.

GEMTESA is marketed in two packaging configurations:

Thirty (30) tablets in a HDPE bottle with a child-resistant cap, NDC 73336-075-30

Ninety (90) tablets in a HDPE bottle with a child-resistant cap, NDC 73336-075-90

Store at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Keep this and all medications out of sight and reach of children.

Dispose unused medication via a take-back option if available; otherwise follow FDA instructions for disposal in the household trash. See www.fda.gov/drugdisposal for more information.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Urinary Retention

Inform patients that GEMTESA has been associated with urinary retention. Inform patients that the risk of urinary retention may be increased in patients taking muscarinic antagonist medications for the treatment of OAB. Instruct patients to contact their healthcare provider if they experience symptoms consistent with urinary retention while

taking GEMTESA [see *Warnings and Precautions (5.1)*].

Angioedema

Inform patients that GEMTESA may cause angioedema. Advise patients to immediately discontinue GEMTESA and seek medical attention if angioedema associated with upper airway swelling occurs as this may be life-threatening [see *Contraindications (4) and Warnings and Precautions (5.2)*].

Administration Instructions

Advise patients that GEMTESA tablets can be swallowed whole with a glass of water or may be crushed, mixed with a tablespoon of applesauce and taken immediately with a glass of water [see *Dosage and Administration (2.1)*].

Manufactured for and Distributed by:

Sumitomo Pharma America, Inc.

Marlborough, MA 01752

◆ is a trademark of Sumitomo Pharma Co., Ltd., used under license.

SUMITOMO PHARMA is a trademark of Sumitomo Pharma Co., Ltd., used under license.

SUMITOMO is a registered trademark of Sumitomo Chemical Co., Ltd., used under license.

Sumitomo Pharma America, Inc. is a U.S. subsidiary of Sumitomo Pharma Co., Ltd.

All other trademarks are the property of their respective owners.



PATIENT INFORMATION

GEMTESA [gem tes' ah]

(vibegron)

tablets, for oral use

What is GEMTESA?

GEMTESA is a prescription medicine used to treat the following symptoms due to a condition called overactive bladder in adults, and in adult males taking medicine for benign prostatic hyperplasia (BPH):

- urge urinary incontinence: a strong need to urinate with leaking or wetting accidents
- urgency: the need to urinate right away
- frequency: urinating often

It is not known if GEMTESA is safe and effective in children.

Do not take GEMTESA if you:

- are allergic to vibegron or any of the ingredients in GEMTESA. See the end of this leaflet for a complete list of ingredients in GEMTESA.

Before you take GEMTESA, tell your doctor about all of your medical conditions, including if you:

have liver problems.

- have kidney problems.
- have trouble emptying your bladder or you have a weak urine stream.

- take medicines that contain digoxin.
- are pregnant or plan to become pregnant. It is not known if GEMTESA will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if GEMTESA passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take GEMTESA.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take GEMTESA?

- Take GEMTESA exactly as your doctor tells you to take it.
- Take 1 GEMTESA tablet, by mouth, 1 time a day with or without food.
- Swallow GEMTESA tablets whole with a glass of water.
- You may also crush GEMTESA tablets, mix with 1 tablespoon (about 15 mL) of applesauce, and take right away with a glass of water.

What are the possible side effects of GEMTESA?

GEMTESA may cause serious side effects, including:

- **inability to empty your bladder (urinary retention).** GEMTESA may increase your chances of not being able to empty your bladder, especially if you have bladder outlet obstruction or take other medicines for treatment of overactive bladder. Tell your doctor right away if you are unable to empty your bladder.
- **angioedema.** GEMTESA may cause an allergic reaction with swelling of the lips, face, tongue, or throat, with or without difficulty breathing and may be life-threatening. Stop using GEMTESA and get emergency medical help right away if you have symptoms of angioedema or trouble breathing.

The most common side effects of GEMTESA include:

- urinary tract infection
- headache
- nasal congestion, sore throat or runny nose
- diarrhea
- nausea
- upper respiratory tract infection

These are not all the possible side effects of GEMTESA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store GEMTESA?

- Store GEMTESA at room temperature between 68°F to 77°F (20°C to 25°C).
- Safely throw away medicine that is no longer needed in your household trash.
- You may also dispose of the unused medicine through a take-back option, if available. See www.fda.gov/drugdisposal for more information.

Keep GEMTESA and all medicines out of the reach of children.

General information about the safe and effective use of GEMTESA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use GEMTESA for a condition for which it was not prescribed. Do not give GEMTESA to other people, even if they have the same symptoms that you

have. It may harm them.

You can ask your doctor or pharmacist for information about GEMTESA that is written for health professionals.

What are the ingredients in GEMTESA?

Active ingredient: vibegron

Inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, mannitol, and microcrystalline cellulose. The light green film coating contains FD&C Blue No. 2 - aluminum lake, hypromellose, iron oxide yellow, lactose monohydrate, titanium dioxide, and triacetin.

Manufactured for and Distributed by:

Sumitomo Pharma America, Inc.

Marlborough, MA 01752

◆ is a trademark of Sumitomo Pharma Co., Ltd., used under license.

SUMITOMO PHARMA is a trademark of Sumitomo Pharma Co., Ltd., used under license.

SUMITOMO is a registered trademark of Sumitomo Chemical Co., Ltd., used under license.

Sumitomo Pharma America, Inc. is a U.S. subsidiary of Sumitomo Pharma Co., Ltd.

All other trademarks are the property of their respective owners.

For more information, go to www.GEMTESA.com or call 1-833-876-8268.



This Patient Information has been approved by the U.S. Food and Drug Administration.

Approved: 12/2024

PRINCIPAL DISPLAY PANEL - 75 mg Tablet Bottle Label

30 tablets

NDC 73336-075-30

Rx Only




GEMTESA®

(vibegron) tablets

75 mg

One Tablet • Once Daily

May be swallowed whole or crushed

30 tablets NDC 73336-075-30 Rx Only	Recommended Dosage: Read full prescribing information This package is child-resistant. Keep this and all medicines out of sight and reach of children. Store at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature] Each tablet contains: 75 mg vibegron Mfd. for: ◆ Sumitomo Pharma Marlborough, MA 01752 Patient resources: gemtesa.com 1-833-876-8268	 3 73336 07530 2	SUM0002 70046005
 One Tablet • Once Daily May be swallowed whole or crushed		GTIN XXXXXXXXXXXXXXXX SN XXXXXXXXXXXXXXXXXXXX EXP YYY-MM LOT XXXXXXX	

GEMTESA

vibegron tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:73336-075
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
vibegron (UNII: M5TSE03W5U) (vibegron - UNII:M5TSE03W5U)	vibegron	75 mg

Inactive Ingredients

Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
croscarmellose sodium (UNII: M28OL1HH48)	
HYDROXYPROPYL CELLULOSE, UNSPECIFIED (UNII: 9XZ8H6N6OH)	
magnesium stearate (UNII: 70097M6I30)	
FD&C BLUE NO. 2 ALUMINUM LAKE (UNII: 4AQJ3LG584)	
lactose monohydrate (UNII: EWQ57Q8I5X)	
hypromellose, unspecified (UNII: 3NXW29V3WO)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
titanium dioxide (UNII: 15FIX9V2JP)	
triacetin (UNII: XHX3C3X673)	

Product Characteristics

Color	GREEN	Score	no score
Shape	OVAL	Size	9mm
Flavor		Imprint Code	V75
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73336-075-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	12/29/2020	
2	NDC:73336-075-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	12/29/2020	
3	NDC:73336-075-07	1 in 1 CARTON	12/29/2020	
3		7 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA213006	12/29/2020	

Labeler - Sumitomo Pharma America, Inc. (131661746)

Revised: 4/2025

Sumitomo Pharma America, Inc.