UROVANT SCIENCES

GEMTESA® (vibegron)
Mechanism of Action

GEMTESA® (vibegron) 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. Please see accompanying full Prescribing Information.

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Mechanism of Action

Vibegron is a novel, highly selective, orally bioavailable agonist for the human beta 3-adrenergic receptor (β3-AR). β3-ARs are widely distributed in humans and are prevalent in adipose tissue where activation metabolizes triglycerides into free fatty acids and glycerol. These receptors are also found in the gallbladder, colon, and are the most prevalent subtype expressed in human bladder detrusor smooth muscle.

Similar to β1-AR, β2-AR subtypes, agonists acting at the membrane-bound β3-AR increases intracellular levels of cyclic adenosine monophosphate *via* activation of guanine nucleotide-binding proteins (G-proteins) and adenylyl cyclase.

In isolated human bladder smooth muscle, activating β3-AR with selective agonists results in smooth muscle relaxation, supporting the potential benefit of β3-AR agonists for treating OAB, a syndrome defined as urinary urgency, usually associated with frequency and nocturia, with or without urge urinary incontinence.

In vitro pharmacology studies demonstrate that vibegron is a highly selective and potent activator of the human β3-AR. Vibegron has >9000-fold selectivity for activation of β3-AR compared to β1- or β2-AR with negligible activation of the human β1- and β2-AR, in cell-based functional assays, and no apparent binding to β1- or β2-AR in competitive binding assays.

Reference

1. NDA 213006 Section 2.4 Nonclinical Overview, October 24, 2019. Urovant Sciences, Irvine, CA.