UROVANT SCIENCES

GEMTESA® (vibegron)
Crushed Tablets

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.[1] Please see accompanying full Prescribing Information.

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.[1]

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.[1]

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Bioequivalence of Crushed Vibegron Tablets

An *in vitro* study compared the bioequivalence of vibegron immediate release (IR) 75 mg tablets clinical trials material (CTM) batches (reference batch) with vibegron IR tablets 75 mg registration batches (test batches).[2]

Vibegron IR 75 mg tablets CTM batch (reference batch) was also compared to vibegron IR 75 mg tablets CTM batch (crushed tablet mixed with 15 mL [1 tablespoon] of applesauce).[2]

Bioequivalence was assessed by comparing the dissolution profiles of the reference and test samples in various dissolution media including 0.1 N HCl; 50 mM acetate buffer, pH 4.5; and 50 mM phosphate buffer, pH 6.8. Twelve samples of each batch was tested.[2]

The average percent of released drug after 15 minutes in all three dissolution media was >85% for both batches and were therefore considered bioequivalent. As expected, drug release occurred more quickly from the crushed tablets mixed in applesauce.[2]

Effect of food on absorption

A 2-part, open-label, randomized, crossover, single dose study assessed the effect of food on vibegron pharmacokinetics and assessed the pharmacokinetics of vibegron crushed in applesauce.[3]

Crushed tablets mixed with applesauce were stored at room temperature (20 - 25ºC) for up to 4 hours.[3]

Vibegron C_{max} and $AUC_{0-\infty}$ decreased 63% and 37% respectively in the presence of a high fat meal compared to administration in the fasted state. Vibegron C_{max} decreased 30% and $AUC_{0-\infty}$ was unchanged when crushed and mixed in a tablespoon of applesauce.[3]

The administration of single-dose vibegron either in a fasted state or with a high fat meal (Part 1) as well as administered intact or crushed in applesauce (Part 2) among healthy adult subjects was generally safe and well tolerated.[3]

In the Phase 2 Study, vibegron was administered without regards to meal and exposures were similar between subjects who took vibegron with or without a meal.[3] Results from the Phase 2 study in addition to the Phase 3 studies where vibegron was also administered without regards to meals demonstrated a favorable safety/tolerability profile.[4,5,6]

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]).[1]

References

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4. Mitcheson HD, Samanta S, Muldowney K, et al. Vibegron (RVT-901/MK-4618/KRP-114V) Administered Once Daily as Monotherapy or Concomitantly with Tolterodine in Patients with an Overactive Bladder: A Multicenter, Phase IIb, Randomized, Double-blind, Controlled Trial. Eur Urol. 2019;75: 274-282.
5. Staskin D, Frankel J, Varano S, et al. International phase III, randomized, double-blind, placebo and active controlled study to evaluate the safety and efficacy of vibegron in patients with symptoms of overactive bladder: EMPOWUR. J Urol. 2020;204:316-324. https://www.auajournals.org/doi/10.1097/JU.0000000000000807
6. Staskin D, Frankel J, Varano S, et al. Once-daily vibegron 75 mg for overactive bladder: long-term safety and efficacy from a double-blind extension study of the international phase 3 trial (EMPOWUR), J Urol. 2020, doi:10.1097/JU.0000000000001574. https://www.auajournals.org/doi/10.1097/JU.0000000000001574