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Plain language summary of safety and symptom improvement with vibegron in people with overactive bladder: results from the EMPOWUR study

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Summary

What is this summary about?

This is a plain language summary of an article originally published in the *Journal of Urology*. Overactive bladder (also called OAB) has been treated with the same type of medicine for more than 40 years. Vibegron is in a newer class of medicine for treating overactive bladder called beta-3 adrenergic receptor agonists. The EMPOWUR study was a phase 3 clinical trial that looked at whether vibegron was safe and improved symptoms in people with overactive bladder. Vibegron was approved by the US Food and Drug Administration (also called the FDA) based in part on the results of this study.

How to say (double click on the sound icon to play the sound)

Vibegron: vye-BEG-rahn
Beta-3 adrenergic receptor: BAY-ta three ah-druh-NUR-jik ree-SEP-tor
Tolterodine: tohl-TEH-ruh-deen
Anticholinergic: an-tee-koh-lin-NUR-jik
Incontinence: in-KAAN-tin-nents

What were the results?

Participants of the EMPOWUR study who took vibegron showed an improvement in their overactive bladder symptoms. These symptoms include the number of urinations (peeing), the urgent need to urinate, and accidental urination (bladder leaks). After 12 weeks, participants who took vibegron had significantly greater improvements than participants who took placebo.

What do the results mean?

This study suggests that vibegron could safely improve symptoms in people with overactive bladder.

Where can I find the original article on which this summary is based?

The original article is called "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." You can read the original article published in the *Journal of Urology* at this link: https://www.auajournals.org/doi/10.1097/JU.0000000000000807

Who is this article for?

This summary may be helpful for adults with overactive bladder who want to better manage their symptoms and understand newer treatment options. Their families, their caregivers, and the healthcare providers who treat these conditions can also benefit from this summary.

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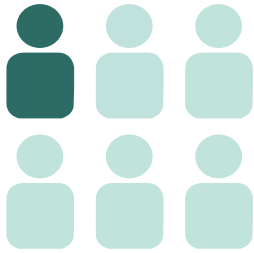
What is overactive bladder?

Adults with overactive bladder, also called OAB, often feel an urgent need to urinate that is difficult to ignore, which can cause accidental urination or leakage. Nearly 1 in 6 adults in the US have overactive bladder. Frequent and suddenly needed bathroom visits can make daily life difficult. Overactive bladder symptoms often result in disruption in daily life. These symptoms can affect sleep, work, and social activities. These disruptions can be very distressing and inconvenient. The number of people with overactive bladder increases with age, and more women are affected than men.



What is vibegron?

Vibegron is a medicine approved by the FDA to treat overactive bladder. It is in a newer class of medicine for treating overactive bladder called **beta-3 adrenergic receptor agonist**. Vibegron is a pill that you take once a day. It is prescribed to people with overactive bladder to help them urinate less often, reduce strong bladder urgency, and have fewer bladder leaks.

Beta-3 adrenergic receptor agonist: An agonist is a substance that can bind to a receptor. A receptor is found either inside or on the surface of a cell. The binding of a particular substance to a receptor can cause an effect in the cell. The beta-3 adrenergic receptor is a type of receptor found in the bladder. When this receptor is activated, the bladder relaxes. Vibegron is a medicine that can bind to this type of receptor.

Why was this study carried out?

Anticholinergic: A type of medicine that blocks the effect of acetylcholine, a type of chemical in the nervous system. When an anticholinergic blocks acetylcholine, it reduces bladder contraction and the strong desire to urinate.
Phase 3 clinical study: A study in which a medicine is taken by participants to test if it can improve health. It is a final type of study needed for approval of a new medicine in the US by the FDA.

Medicines need to be tested to be approved by the FDA so they can be prescribed in the US. Many people with overactive bladder are treated with a type of medicine called an **anticholinergic**. Some people dislike taking these medicines because they are bothered by side effects. These side effects include dry mouth, blurred vision, heartburn, dry skin, and constipation. Anticholinergic medicines may increase the risk of dementia. Tolterodine is an example of an anticholinergic medicine used for overactive bladder. Vibegron works differently than anticholinergic medicines.

The EMPOWUR study was a **phase 3 clinical study** that looked at how safe vibegron is and how successful it is at reducing overactive bladder symptoms.

How was this study carried out?

1518 participants volunteered to take part in the EMPOWUR study. Each participant had to be 18 years old or older and had to have overactive bladder for at least 3 months.

1518 participants

The participants were randomly divided into 3 groups. They were given a pill to take once a day: vibegron, **placebo**, or another medicine called tolterodine (an anticholinergic). Tolterodine was used as an **active control**.

The study was **double blinded**, which means that neither the participants nor the researchers knew which pill was being given.

540 participants Placebo

5:5

547 participants Vibegron

5:4

431 participants Tolterodine

Participants took their assigned medicine for 12 weeks.

Placebo: A pill with no medicine in it. This is sometimes called a "sugar pill". In some studies, participants may be assigned to take a placebo rather than the study medication.
Active control: An approved medicine to which results can be compared. In this study, both the medicine of interest (vibegron) and the active control (tolterodine) were compared to placebo.
Double blinded: A study in which neither the participant nor the researcher knows which treatment a participant has been given. The treatment groups in this study were vibegron (the new drug being tested), tolterodine (the active control), or placebo.

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Participants answered questions in a 7-day paper diary at 1 and 3 weeks before starting their study medicine and before study visits at weeks 2, 4, 8, and 12.

The main results researchers were interested in were:

The change in number of **urination episodes**	The number of episodes of **bladder leakage** with the urgent need to urinate (called urge urinary incontinence or accidental bladder leakage)	The number of episodes of a sudden, intense need to urinate (**urgency episodes**)
Urination episode: A time that the participant urinated (peed).	**Bladder leakage:** A time when accidental peeing happened because of an intense need to urinate and not making it to the toilet in time. Any accidental peeing episodes not related to urgency were not counted.	**Urgency episode:** A time that the participant felt a sudden and intense desire to pee right now.

These outcomes were compared between all participants who took vibegron and placebo and between participants who took tolterodine and placebo. This study did not compare vibegron to tolterodine.

Researchers were also interested in safety:

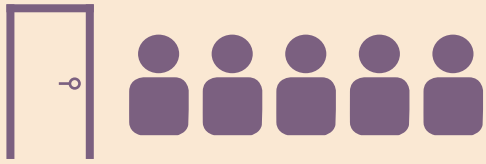
Researchers recorded **adverse events** and **serious adverse events** reported by participants to determine if vibegron is safe to use. A researcher will decide if the adverse event was a side effect of taking the medicine.

Adverse event: Any undesirable experience that occurs during use of a medicine during a clinical trial. Adverse events can range from mild to severe and may not be related to the medicine being used.	**Serious adverse event:** An adverse event is serious when hospital care is needed or if the event causes disability or permanent damage.

Who took part in the EMPOWUR study?

Participants were from 199 clinical study locations in the US, Canada, Poland, Hungary, Latvia, and Lithuania. Most participants (90%) were from the US.

Characteristics between participants in all 3 groups were similar at the start of the study.



1518 participants with overactive bladder

85% of participants were women

43% of participants were over the age of 65

Urinations per day (average)

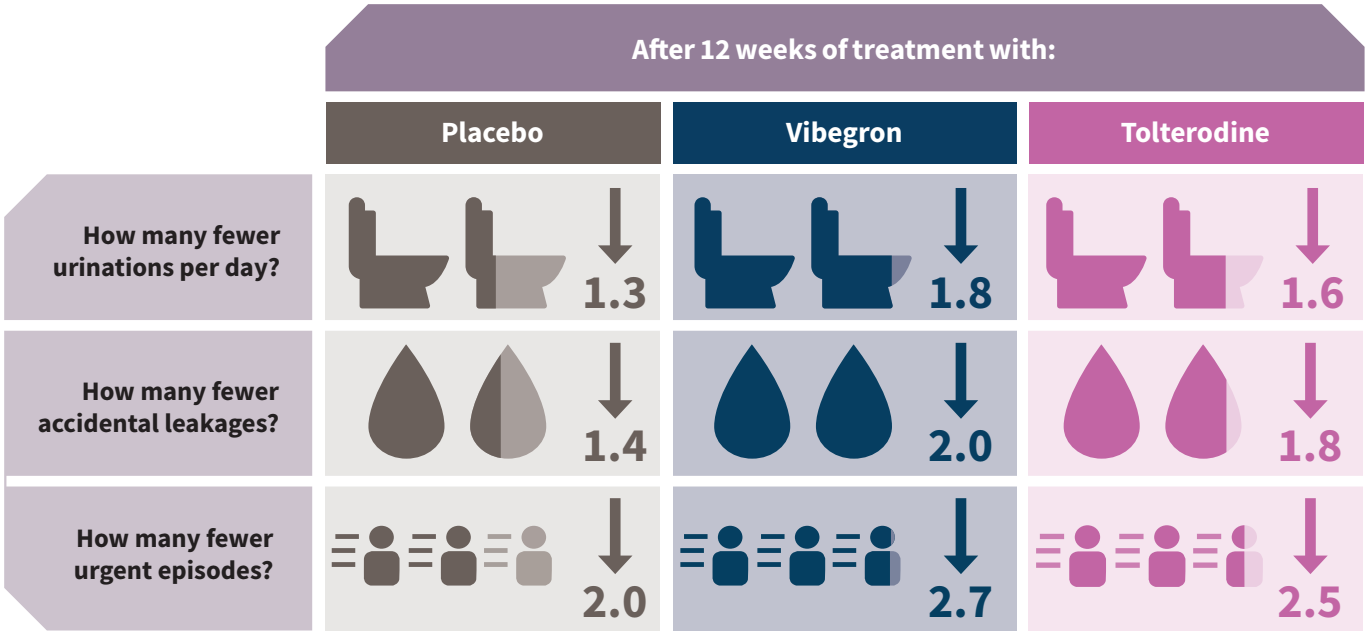
Bladder leaks per day (average)

Urgency epsiodes per day (average)

What were the overall results of the study?

Results showed that vibegron led to fewer urination episodes per day with 12 weeks of treatment. For example, participants who took a placebo pill had an average of over 1 fewer urinations per day by the end of the study. Participants who took vibegron had an average of almost 2 fewer times they needed to urinate by the end of the study. Vibegron also led to a decrease in accidental leakages per day and in the total number of urgency episodes per day. These decreases could lead to more time available during the day for activities when fewer bathroom visits are needed.

After 12 weeks of treatment with:



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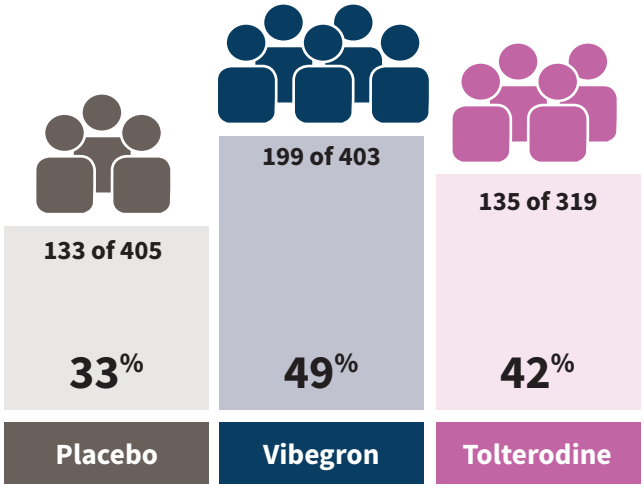
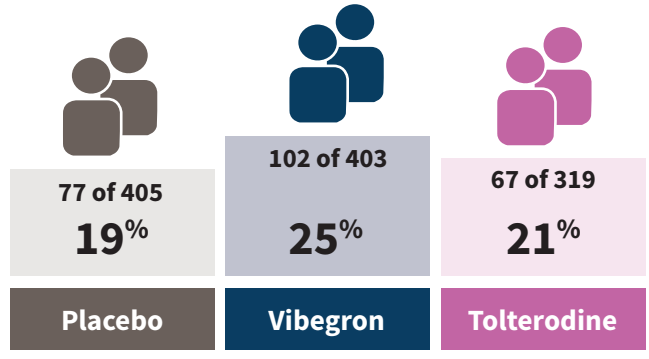
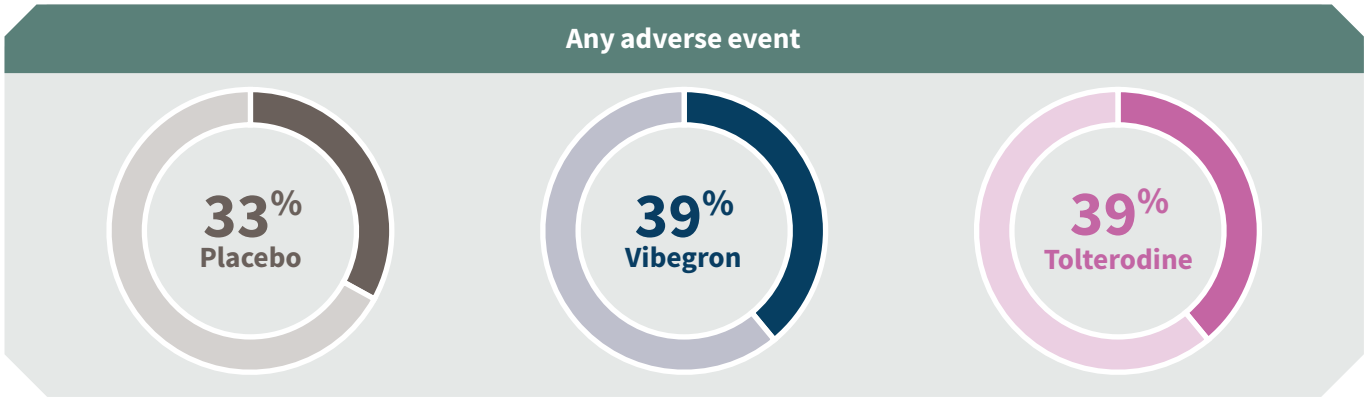
Almost half (49%) of participants taking vibegron saw a 75% decrease in the number of accidental leakage episodes with vibegron. After taking vibegron, 25% of participants experienced no accidental leakage episodes at all (100% decrease).





What were the most common side effects?

Participants from each treatment group reported adverse events, shown below. The most frequent adverse event was dry mouth. Dry mouth is a common side effect of anticholinergic medicines like tolterodine.



	Common adverse events		
	Placebo	Vibegron	Tolterodine
Urinary tract infection	6%	5%	6%
Headache	2%	4%	3%
Nasopharyngitis (common cold)	2%	3%	3%
Diarrhea	1%	2%	2%
Constipation	1%	2%	1%
Dry mouth	1%	2%	7%
Hypertension (high blood pressure)	2%	2%	3%
Nausea	1%	2%	1%
Upper respiratory tract infection	1%	2%	1%

What do the results of this study mean?

- The EMPOWUR study showed that vibegron decreased the number of times a participant needed to urinate each day, decreased daily episodes of accidental leakage, and decreased the number of daily urgency episodes over the course of 12 weeks of treatment.
- The number and types of adverse events participants had while taking vibegron was similar to placebo, which suggests that vibegron is safe to use.
- The EMPOWUR trial was one of the phase 3 clinical trials that led to approval of vibegron by the FDA.

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Where can readers find more information on these studies?

The original article is called "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." It was published in the *Journal of Urology* in 2020. This paper is free to access. You can access the paper using the link below:

- https://www.auajournals.org/doi/10.1097/JU.0000000000000807

Information on the trial itself can be accessed using the link below:

- https://clinicaltrials.gov/ct2/show/NCT03492281

Who sponsored these studies?

Sumitomo Pharma America, Inc. (formerly Urovant Sciences, Inc.), the maker of vibegron, supported this work.

Financial and competing interests disclosure

David Staskin, MD, is a consultant for Astellas, AzuraBio, UroCure, and Sumitomo Pharma America (formerly Urovant Sciences); is an investigator and meeting participant/lecturer for Astellas and Sumitomo Pharma America (formerly Urovant Sciences); and holds other interests in AzuraBio and UroCure. Jeffrey Frankel, MD, is an advisor for Sumitomo Pharma America (formerly Urovant Sciences); a meeting participant/lecturer for Myovant, Pfizer, and Sumitomo Pharma America (formerly Urovant Sciences); and is an investigator for Exact Sciences, Johnson & Johnson, and Pfizer. Steven G Gregg, PhD, is Executive Director at the National Association for Continence, Charleston, SC. Susann Varano, MD, is a consultant and speaker for Sumitomo Pharma America (formerly Urovant Sciences), is a principal investigator for Clinical Research Consulting, and holds academic positions at Sacred Heart University and University of Bridgeport. Janet Owens-Grillo, PhD, MS, is an employee of Sumitomo Pharma America (formerly Urovant Sciences).

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