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# The Study Of Efficacy & Safety Of Mirabegron & Vibegron In Treatment Of Overactive Bladder

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## Abstract :

Mirabegron opened a new period in the treatment of hyperactive bladder( OAB) For the first time croakerealing with OAB have an effective volition to the pharmacological dependence of the remedy for this complaint, the antimuscarinic medicines. This first- by- class, potent β3- adrenoceptors agonist has lately entered blessing by nonsupervisory authorities in Japan, United States and Europe, grounded on the favourable efficacity- tolerability profile demonstrated in multiple randomized, transnational, controlled trials, both short and long- term. Mirabegron is a novel, formerly- daily, orally active, first- in- class, potent β3- adrenoceptor agonist lately approved by Food and Drug Administration for hyperactive bladder remedy. Phase II studies and four large- scale phase III transnational randomized, controlled trials have supported the efficacity and tolerability of mirabegron & vibegron in the clinical trial setting of cases with hyperactive bladder for over to 12 weeks of remedy and in the long term( 12 months). The reported prevalence and inflexibility of treatment- emergent and serious adverse goods were analogous to antimuscarinics.

Vibegron is, in discrepancy to other OAB medicines, veritably picky and leads to a lower degree of unwanted side goods. Vibegron is set up to be a substrate for CYP3A4 in vivo, but doesn't actually induce or inhibit any of the cytochrome P450 enzymes and is therefore less likely to take part in medicine – medicine relations( DDI). Then vibegron differs from the former hyperactive bladder medicine mirabegron, which was known to be associated in colorful medicine – medicine relations.

## Keywords :

*Mirabegron , vibegron , antimuscarinic Agent , β3- adrenoceptor Agonist ,Overactive Bladder*

## Introduction:

Overactive bladder( OAB) is a syndrome characterized by the crucial symptom of urinary urgency, with or without urinary incontinence, generally associated with urinary frequence and nocturia. Detrusor muscle overactivity( DO) is frequently, but not always, the underpinning condition. The discriminational opinion with stress or mixed urinary incontinence, grounded on clinical examination and urodynamic examinations, is of utmost significance in order to plan the more applicable remedial strategy.[1-3]

The treatment of OAB is aimed to achieve symptom relief and enhancement of HRQL. First- line treatment relies substantially on life advice and bladder training, functional electrical stimulation, clean intermittent catheterization and pharmacological treatment Neuromodulation, intradetrusor botulinum poison injection and surgery represent morei. nvasive, alternate- line treatment options. Antimuscarinics are the dependence in the pharmacological treatment ofOAB.However, antimuscarinics aren't fully bladder- picky causing bothersome adverse goods( AEs), Includeing dry- mouth, nausea, constipation. [4-7]


**figure 1 : - schematic representation of overactive bladder**

***Female sexual dysfunction (FSD)*** is traditionally classi- fied into diseases of desire, thrill, lubrication, orgasmand pain. In the absence of detailed epidemiologicaldata, current estimates have up to 43 of women com- plaining of at least one sexual issue. Women are at threat of developing FSD due to physiologic, iatrogenicand cerebral factors. Lower tract urinary tract in- fections are a further, independent FSD cause, To identify FSD, applicable assessment guideline should be applied. So as to ascertain sexual history and enable assessment, there are a number of tone- reporting questionnaires available. The womanish Sexual FunctionIndex( FSFI) is a terse, multidimensional " gold stage- ard " tool which is regarded in high-regard.[8-10]

## Anatomy Of Urinary Bladder

Urinary bladder is a sac like muscular structure, which is present under the peritoneum, at the reverse of pubic bones and located on the bottom of the pelvic depression. The bladder actsas a force for urine collection and executes micturition process by coordinating storing and voiding cycle. Urinary bladder is aligned with detrusor muscle and its compression is responsible for micturition. The urinary bladder consists of ureter perforations, the triangular shaped trigone, and the internal perforation. The whole micturition cycle involves two phases videlicet storehouse phase and voiding phase.. Both phases are coordinated by sympathetic and parasympathetic neuronal system. In general, prefrontal cortex laterally controls voluntary voiding phase. [11- 13]

## Overactive bladder :

Overactive bladder ( OAB) is defined by the International Continence Society( ICS) as urinary urgency in theabsence of any given infection or other egregious pathology. OAB is generally characterizeod by frequence and nocturia, but may or may not beget urinary Badder.

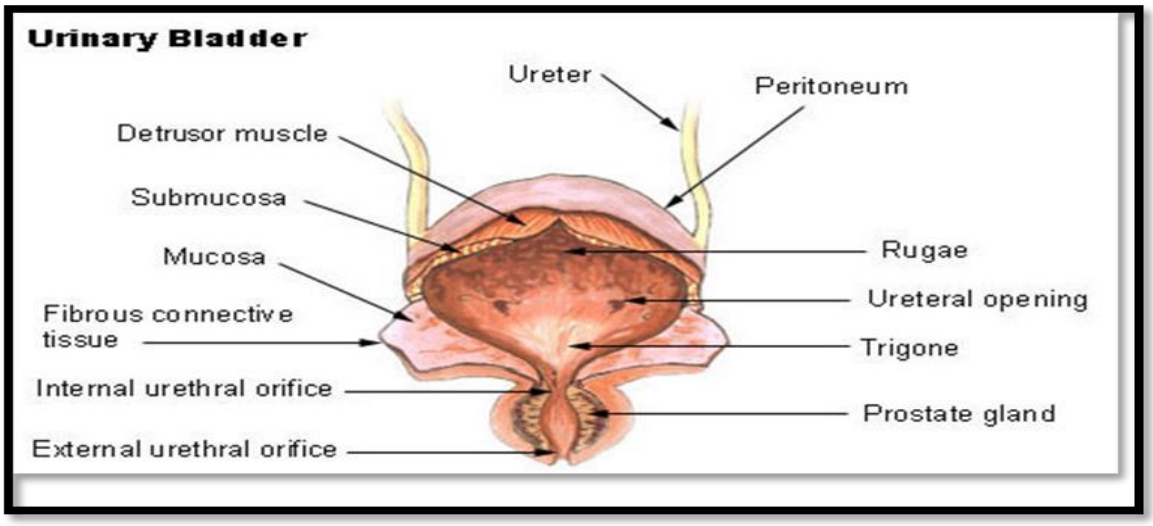



**figure 2 :- anatomy of urinary bladder**

## Mechanism of overactive bladder :

Activation of muscarinic receptor is responsible for normal compression of urinary bladder which is essential for evacuating or voiding during voluntary urination.The voiding phase of urinary cycle is coordinated by parasympathetic system, which secretes acetylcholine( Ach) neurotransmitter and activates M2 and M3 receptors. in unnatural detrusor muscle condensation, which might be responsible for the OAB pattern.[15]

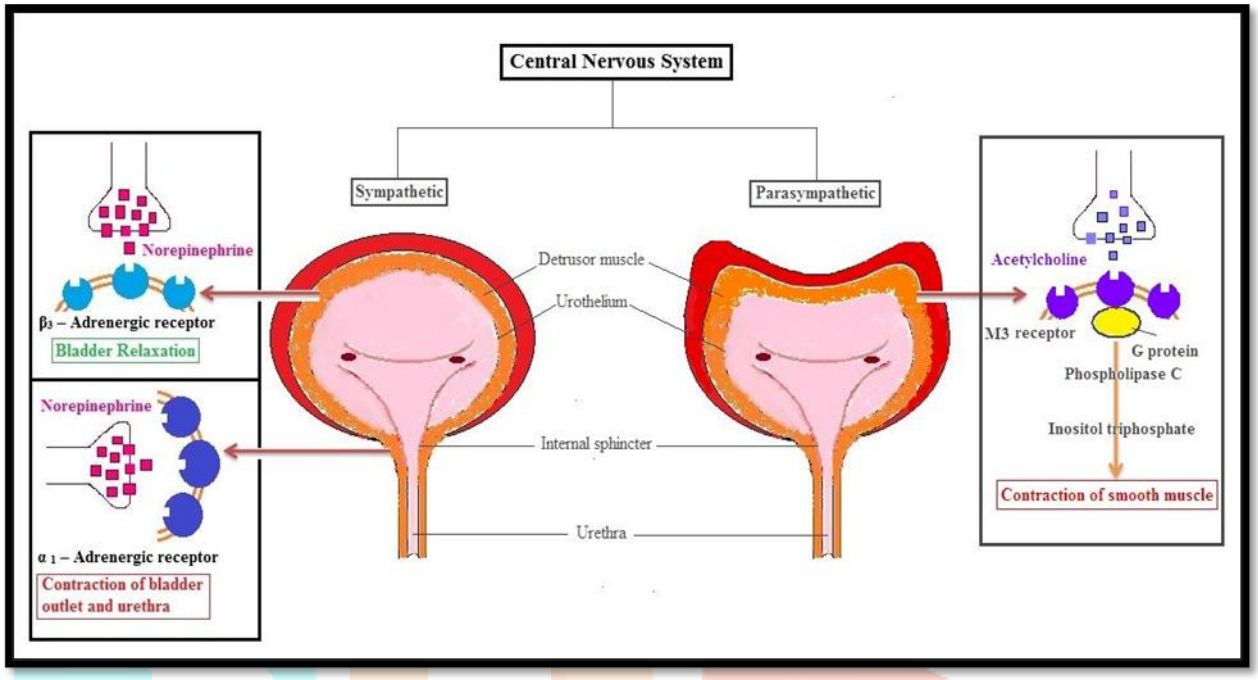



**figure 3:- mechanism of overactive bladder**

## Management of OAB

### *Step 1: Conservative management*

Conservative measures re a reasonable first- line operation strategy depending on the burden of complaint faced by the case. Communication with and education of the case, and potentially caregivers, is important with early operation. It's necessary to laboriously engage the case to agree on interventions or modifying behaviours that are doable. near compliance with conservative measures has an efficacity of 50.

Specifically, conservative measures include;

- treatmentof adjustable threat factors( eg weight reduction)
- reduction of exposure to bladder instigations( eg alcohol, caffeine, smoking, carbonated potables)
- constipation avoidance – aiming for soft droppings passing every 2 days; case adding diurnal fibre input; potentially using coprolite mufflers and laxative

[16- 18]

### *Step 2 : Pharmacotherapy*

#### *Anticholinergic remedy*

Anticholinergic specifics block the acetylcholine neurotransmitter synapse in the central and supplemental nervous systems, inhibiting parasympathetic exertion, thereby reducing the involuntary movement of smooth muscles similar as those present in the bladder. Multiple anticholinergic specifics are available for use in clinical practice. similar specifics includenon-selective agents( oxybutynin, tolterodine) or more- picky agents( solifenacin, darifenacin).[19- 20]

#### *Beta-adrenergic remedy*

It receptor agonists upregulate sympathetic exertion, thereby promoting detrusor smooth muscle relaxation and accordingly reducing muscle spasms The current commercially available β3 adrenoceptor agonist is mirabegron. It works via a different path to anticholinergic agent by relaxing the detrusor muscle, allowing advanced bladder volumes before the need for urination.[ 21]

## Drugs For Treatment Of OAB :

In people with hyperactive bladder, muscles in the bladder wall contract at the wrong time. A group of medicines called anticholinergics combat this problem by blocking the whim-whams signals related to bladder muscle condensation. Research suggests that these medicines also might increase bladder capacity and drop the appetite to go.

***Anticholinergic medicines include***

• Darifenacin( Enablex)

• Fesoterodine( Toviaz)

• Oxybutynin( Ditropan, Ditropan XL, Gelnique, Oxytrol)

Solifenacin( Vesicare)

• Tolterodine( Detrol, Detrol LA)

• Trospium( Sanctura)

Oxytrol for women is the only medicine available over the counter. Overall, these medicines work about the same in treating hyperactive bladder, and generally people tolerate all of them well. The main side effect is dry mouth, but anticholinergics also can beget constipation, blurred vision, and increased twinkle.

Croakers also treat men with medicines that relax a muscle at the bladder neck and prostate to help with evacuating.

They include

• Alfuzosin( Uroxatral)

• Doxazosin( Cardura, Cardura XL)

• Silodosin( Rapaflo)

• Tamsulosin( Flomax)

• Terazosin( Hytrin) [22]

## New Developments :

***Potassium channel opening Agents***

This agents induce the opening of K ion channels in the detrusor muscle cell membrane, which results in hyperpolarization and muscle relaxation. US Food and Drug Administration( FDA) approved the antimuscarinic medicines as a dependence drug for OAB symptoms. Unfortunately, antimuscarinics paradenon-selective action on the muscarinic receptor, which redounded in poor efficacity.

Recent developments in the understanding of the pathophysiology of OAB have accelerated abecedarian and clinical exploration leading to the discovery of new class of composites. Among them, β3- adrenoceptor( AR) agonists appear to be veritably effective in the treatment of OAB.

**Mirabegron (YM178) is** β3 AR agonist, first-in-class, potent orally active drug in this category Mirabegron was granted marketing approval in Japan (July 2011), and was launched in *September 2011*. FDA also approved mirabegron **Myrbetriq,** Astellas Pharma US, Inc.) in June 2012.[23-25]

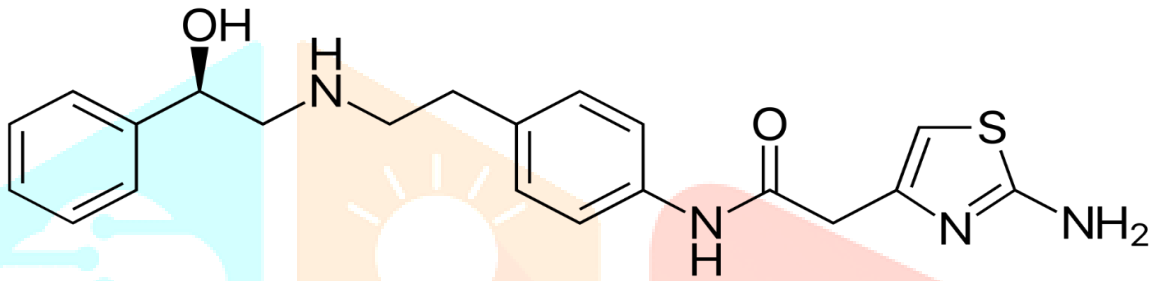
**Vibegron**, is an oral, once-daily (75 mg) small molecule beta-3 agonist for the treatment of adult patients with overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency. **GEMTESA** was approved by the U.S. FDA in December 2020 and launched in the U.S. in *April 2021*. GEMTESA is also being evaluated for the treatment of OAB in men with benign prostatic hyperplasia.[26]

## Mirabegron

Mirabegron is a potent and picky agonist of the mortal β3-adrenoreceptor and has low natural exertion for mortal β1 and β2 adreno- receptor. It's the first commercially available β3- agonist medicine certified for the treatment of OAB and has been approved for use in Japan( 2011), the US, Canada( 2012) and Europe( 2013)

Mirabegron shows a distinct mode of action, i.e., targeting β3 adrenoreceptors and ameliorate bladder storehouse without altering void condensation. also mirabegron appears an applicable volition to antimuscarinics, owing to bettered safety profile, limited side goods, high efficacity and tolerability. still, long- term clinical studies and analysis are demanded for assessing the safety, tolerebility and efficacity profile of mirabegron. The expansive clinical trials demonstrated safety and clinical efficacity volition to antimuscarinic remedy. [27-29]

## Structure :




**Synonyms : (YM-178)**

**Generic Name :** Mirabegron

**Brand Name :** Myrbetriq (***Dr.Reddy)***

**Molecular Weight :** 396.5 g/mol

**Molecular Formula :** $C_{21}H_{24}N_4O_2S$


**Image No.1**

## Mechanism of action :

Mirabegron is a potent and picky beta3- adrenoceptor agonist. Mirabegron showed relaxation of bladder smooth muscle in rat and mortal isolated towel, increased cyclic adenosine monophosphate( cAMP) attention in rat bladder towel and showed a bladder relaxant effect in rat urinary bladder function models.[30]

The mortal bladder expresses colorful sympathetic and parasympathetic receptors to help regulate micturition. Activation of the parasympathetic system will affect in bladder compression. Receptors appreciatively affecting bladder compression and micturition include the M2 and M3 receptor subtypes, which serve via the parasympathetic nervous system. These receptors work to increase intracellular calcium and down- regulate cyclic- adenosine, independently, which will increase muscle compression. Negatively affecting micturition generally includes the sympathetic beta- 3 adrenergic receptors. Mirabegron is a beta- 3 receptor agonist which will beget detrusor muscle relaxation. Beast studies have shown that beta- 3 receptor agonists parade a cure-dependent detrusor relaxation( intermediated via up- regulation of cyclic- adenosine) during the storehouse phase of micturition. This way, mirabegron can prop in the characteristic relief of OAB and symptoms of appetite urinary incontinence, urgency, urine frequence .[31-32]

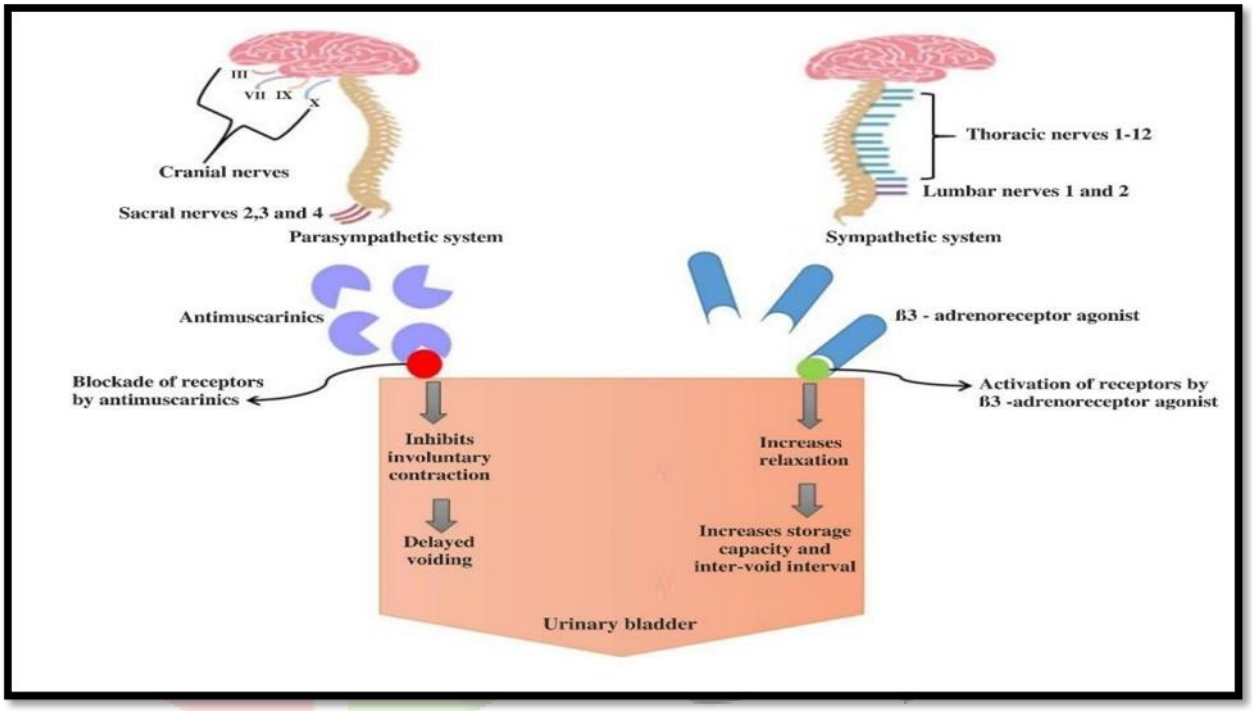



**figure 4 :- mechanism of action of mirabegron**

## Pharmacokinetics :

***Absorption :***

According to the manufacturer's product labeling, mirabegron reaches maximum tube attention( Cmax) at roughly3.5 hours. Steady- state attention are achieved within seven days. In grown-ups, there are no clinically significant differences in mirabegron pharmacokinetics when administered with or without food. still, in pediatric cases, dieted Cmax and AUC increased by 170 and 80,(%) independently, compared to the fed state following the administration of mirabegron granules.

***Distribution :***

Mirabegron has an expansive distribution with the volume of distribution at steady- state( Vss) 1670L. Mirabegron is bound( roughly 71%) to mortal tube proteins, including albumin and nascence- 1 acid glycoprotein. Mirabegron distributes to erythrocytes. Mirabegron volume of distribution is fairly advanced in pediatric cases and is commensurable to body weight.

***Metabolism :***

Mirabegron is metabolized in the liver via multiple pathways involving dealkylation, oxidation, glucuronidation, and hydrolysis. Metabolites aren't pharmacologically active. Studies have also shown the involvement of butyryl cholinesterase, and UGT in the metabolism of mirabegron, in addition to CYP3A4 and CYP2D6. In poor metabolizers of CYP2D6, mean Cmax and AUC are roughly 16% and 17% advanced than in expansive metabolizers of CYP2D6.

***Excretion :***

The mean elimination half- life( t1/ 2) of mirabegron is roughly 50 hours in adult cases and 26 to 31 hours in pediatric cases( mirabegron grains). Renal elimination of mirabegron is primarily through active tubular stashing and glomerular filtration. roughly 55 is excreted in the urine, 34 % in the feces, and 25 % in the urine( unchanged).

## Pharmacodynamics :

Mirabegron exerts its pharmacologic goods by forcing bladder smooth muscle to relax, thereby expanding its capacity and relieving urgency. Mirabegron doesn't appear to negatively affect the mean outside inflow rate or mean detrusor pressure at outside inflow rate in cases with lower urinary tract symptoms and bladder outlet inhibition( jeer), but should be used with in cases with jeer due to reports of significant urinary retention. likewise, mirabegron increases both blood pressure and heart rate in a cure-dependent manner and should thus be used with caution in cases with oppressively unbridled hypertension or others for whom these increases may prove dangerous.[33]

## Adminstration :

Mirabegron is a formerly- diurnal orally administered medicine. It's available in 25 mg or 50 mg strengths. The lower- strength tablet is recommended as a starting cure for cases with severe renal or moderate hepatic impairment. The advanced cure tablet is recommended for cases to take with or without food if they tolerate the lower cure. Other remedial routes of administration( intravenous, rectal, enteral, epidural, intracerebral,etc.) for mirabegron aren't FDA- approved in the treatment of OAB. Mirabegron may take 4 to 8 weeks before cases see advancements in their symptoms. Mirabegron is available in extended- release tablets, extended- release grains, and as an oral suspense.[ 34- 35]

## Half life :

The mean terminal elimination half- life of mirabegron in grown-ups being treated for hyperactive bladder is roughly 50 hours.6 In pediatric cases entering the scrap expression for the treatment of neurogenic detrusor overactivity, the mean terminal elimination half- life is roughly 26- 31 hours .

## Clearance :

Total plasma clearance following intravenous administration is roughly 57 L/ h, with renal clearance account for roughly 25 at roughly 13 L/h.

## Toxicity :

At boluses of over to 400 mg in healthy levies( ~8x the recommended outside), reported symptoms of overdose included palpitations and increased heart rate .

## Adverse effect :

Adverse drug reactions to mirabegron are generally mild and tolerable. One study showed that the adverse goods of mirabegron include hypertension( most generally), nasopharyngitis, and urinary tract infection. Dry mouth( a common side effect ofanti-muscarinic) issix-fold less in mirabegron because mirabegron doesn't affect the muscarinic receptors in the salivaryglands.Other side goods include tachycardia, headache, back pain, dizziness, palpitations atrial fibrillation, urticarial response, common pain, and swelling.[36]

## Contraindications :-

Previous hypersensitivity reaction to mirabegron or any excipients of tablet or oral suspense is a contraindication to mirabegron use. Mirabegron use correlates with hypertension, and its contraindication includes severe unbridled hypertension. Mirabegron is now contraindicated in cases with severe unbridled hypertension( systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 110 mm Hg, or both).[37]

## Medicinal uses :-

- Mirabegron is used alone or together with other drugs( eg, solifenacin succinate) to treat the symptoms of an hyperactive bladder( OAB), similar as incontinence( loss of bladder control), a strong need to urinate right down, or a frequent need to urinate.
- It's also used to treat neurogenic detrusor overactivity( NDO). Mirabegron works on the muscles of the bladder to increase the quantum of urine your bladder can hold and help them from causing incontinence.

## Drug interactions :-

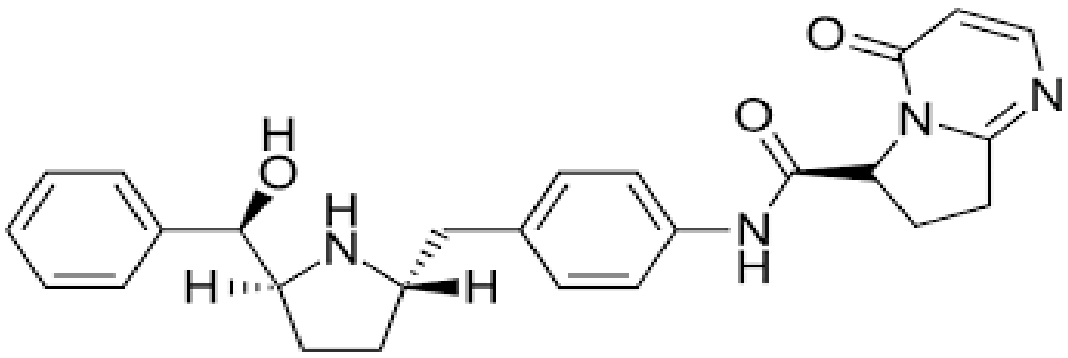
***Drug Metabolized by CYP2D6*** **:** Mirabegron is a moderate asset of CYP2D6. Applicable monitoring is recommended and cure adaptation may be necessary for narrow remedial indicator CYP2D6 substrates.

***Digoxin*** **:** When initiating a combination of Mirabegron and digoxin, define the smallest cure of digoxin; examiner serum digoxin attention to titrate digoxin cure to asked clinical effect.[38]

## Vibegron

Vibegron is, in contrast to other OAB drugs, very selective and leads to a lesser degree of unwanted side effects. Vibegron is found to be a substrate for CYP3A4 in vivo, but does not actually induce or inhibit any of the cytochrome P450 enzymes and is thus less likely to take part in drug–drug interactions (DDI). Here vibegron differs from the previous overactive bladder drug mirabegron, which was known to be associated in various drug–drug interactions by inhibiting CYP2D6 or inducing CYP3A4, CYP2D6 and CYP2C9 in the liver.

Using vibegron only (monotherapy) has positive effects on OAB and UUI, but a combination with other drugs can have additional effects. In a study with antimuscarinic drugs, more DDIs were investigated using a model of rhesus monkeys.[39-43]




## Structure :-

**Synonyms :- KRP-114V, MK-4618, RVT-901, URO-901**

**Generic name :-** Vibegron

**Brand name :** - Gemtesa ***( Anant pharmaceuticals PVT , Ltd )***

**Molecular Weight :-** 444.535 g·mol−1

**Molecular Formula :-** $C_{26}H_{28}N_4O_3$


**Image No. 2**

## 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 receptors compared to beta-1 and beta receptors.v ibegron is a selective agonist for the beta-3 adrenergic receptor. The receptors are located in the feathers, urinary tract and bladder towel. Upon binding, the β3 receptor undergoes a conformational change. This induces the activation of adenylate cyclases via G proteins and thereby promotes the conformation of cyclic adenosine monophosphate( cAMP). The consequence of this waterfall is an increased intracellular cAMP attention, which triggers activation of cAMP-dependent protein kinase A and causes a reduction of Ca2 attention in the cytoplasm.

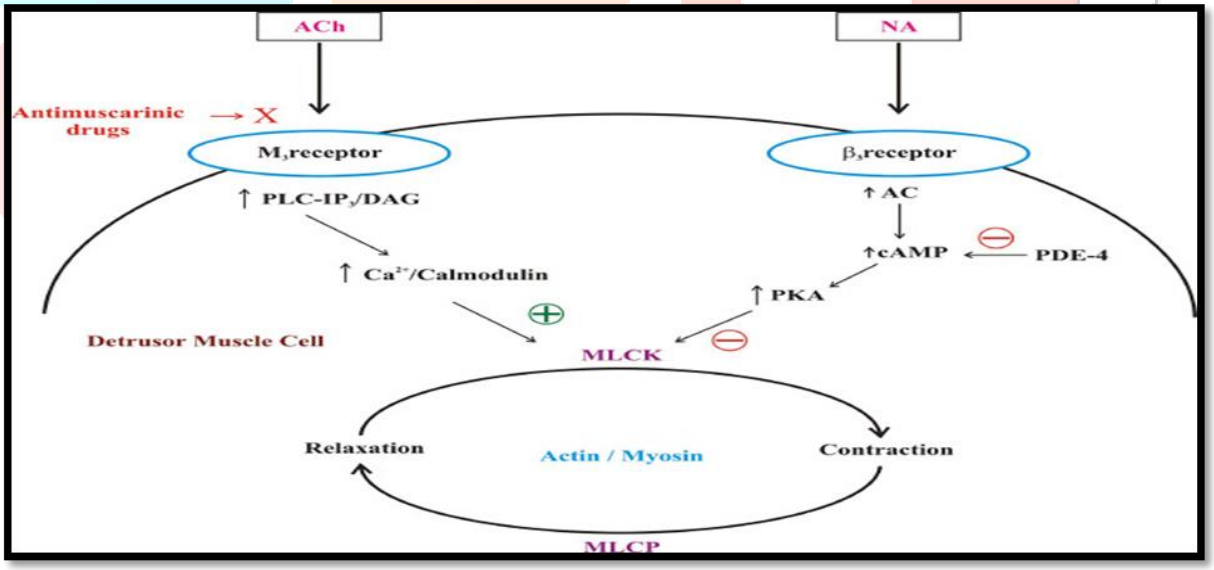



**Figure 5 :- Mechanism Of Action Of Vibegron**

The kinase also phosphorylates myosin chains and thereby inhibits musclecontraction.The final effect of vibegron is muscle relaxation in the bladder. Due to this muscle relaxation bladder capacity increases and symptoms of hyperactive bladder. [44-45]

## Pharmacokinetics :-

***Absorption :-***

The mean Tmax is 1- 3 hours. Steady- state attention are achieved within 7 days of formerly- diurnal dosing Oral administration of a 75 mg vibegron tablet crushed and mixed with 15 mL of applesauce redounded in no clinically applicable changes in vibegron pharmacokinetics when compared to administration of an complete 75 mg vibegron tablet.

***Distribution :-***

The mean apparent volume of distribution is 6304 liters. mortal tube protein list of vibegron is roughly 50. The average blood- to- tube attention rate is0.9.[46]

***Metabolism :-***

In vitro, CYP3A4 is the main enzyme responsible for the metabolism of vibegron, which plays a minor part in the elimination of vibegron. Two predominant metabolic pathways are oxidation and glucuronidation to form two oxidative metabolites and three glucuronide metabolites.4 Metabolites haven't been completely characterized .[47]

***Excretion :-***

Radiolabeled cure, roughly 59 %of the cure( 54 %as unchanged) was recovered in feces and 20%( 19% as unchanged) in urine.

## Pharmacodynamics :-

Vibegron selectivity for beta- 3 adrenergic receptors is> 9000 times advanced than for β1AR or β2AR.4 Vibegron improves clinical symptoms of hyperactive bladder by adding bladder capacity without affecting bladder compression. It significantly increases the functional bladder volume in a cure-dependent manner, which results in extension of the interval between voids. In clinical studies, vibegron inhibited detrusor bladder condensation in a attention-dependent manner, reduced voiding pressure, and increased bladdercompliance.In Japanese clinical studies comprising cases with hyperactive bladder, vibegron significantly bettered the frequence of micturition, urgency, and urgency incontinence occurrences .[43,44,48]

## Adminstrations :-

***Adult Dosing***

Vibegron is cured at one 75 mg tablet by mouth formerly daily for the treatment of OAB with symptoms of appetite urinary incontinence, urinary urgency, and urinary frequence. Can be given with or without food. Swallow the tablet whole with water or crush the tablets and mix with applesauce.

***Pediatrics***

The use of vibegron in patients less than 18 years of age is not recommended.

***Elderly***

Vibegron is cured at one 75 mg tablet by mouth formerly daily for the treatment of OAB with symptoms of appetite urinary incontinence.

## Half-life :-

Vibegron has an effective half- life of30.8 hours across all populations. The terminal tube half- life ranges from 60 to 70 hour [49]

## Clearance :-

There is limited information on the clearance rate of vibegron.

## Toxicity :-

***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.

***Mutagenesis***

Vibegron wasn't mutagenic in in vitro microbial rear mutation assays, showed no substantiation of genotoxic exertion in an in vitro mortal supplemental blood lymphocyte chromosomal aberration assay, and didn't increase the frequence of micronucleated chromatic erythrocytes in an in vivo rat bone gist micronucleus assay.

## *Impairment of Fertility:-*

General toxin, dropped fecundity, and dropped fertility were observed in womanish rats at 1000 mg/ kg/ day, associated with estimated systemic exposure1867-fold advanced than in humans treated with the recommended diurnal cure of GEMTESA .[49]

## Adverse effects :-

The most common side goods of vibegron are dry mouth, constipation, headache, nasopharyngitis, diarrhea, nausea, bronchitis, urinary tract infection and upper respiratory tract infection. In case of urinary retention, the case should stop using the medicine. threat assessment for the medicine in pregnant people has yet to be estimated. adverse goods that passed more constantly with vibegron than with placebo in EMPOWUR were headache(4.0% vs2.4%) and nasopharyngitis(2.8% vs1.7%). The prevalence of hypertension was1.7 %I [50-51]

## Contraindications :-

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

## Medical uses :-

- Vibegron is indicated for the treatment of hyperactive bladder with symptoms of appetite urinary incontinence, urgency, and urinary frequence in grown-ups.
- Gemtesa helps ameliorate
- appetite urinary incontinence a strong need to urinate with oohing or wetting down accidents
- urgency ; the need to urinate right down and
- frequence ; urinating frequently.

## Veterinary uses :-

Pregnant rats were given veritably high daily oral boluses of vibegron during the period of organogenesis and showed no embryo- fetal experimental toxin up to 300 mg/ kg/ day. analogous data was set up in rabbits. motherly toxin was observed when boluses exceeded 100 mg/ kg/ day in lactating rats. Clinical studies show that vibegron isn't poisonous, safe and well- permitted in cases .[51]

## Drug interactions :-

***Digoxin :-***

Taking vibegron with an anticholinergic medicine could increase the threat of urinary retention. attendant use of vibegron increased the Cmax and AUC of digoxin by 21 % and 11%, independently.

***Mirabegron :-***

It may increase the smooth muscle relaxing conditioning of Vibegron. Vibegron is, in discrepancy to other OAB medicines, veritably picky and leads to a lower degree of unwanted side goods. Vibegron is set up to be a substrate for CYP3A4 in vivo, but doesn't actually induce or inhibit any of the cytochrome P450 enzymes and is therefore less likely to take part in drug – drug interactions . [52]

## ❖ Comparisions of mirabegron and vibegron :-

| Information | Mirabegron (Myrbetriq) | Gemtesa(vibegron) |
|---|---|---|
| **First Approval Date** | **June 28, 2012** | **December 23, 2020** |
| **Drug Class** | Urinary antispasmodics | Urinary antispasmodics |
| **Dosage Form(s) Available** | • Oral suspension, extended release<br>• Oral tablet, extended release | • Oral tablet |
| **Pricing** | • Quantity 30 tablet, extended release<br>• Dosage 25 mg<br>• Per Unit $16.00<br>• Cost $480.09 | • Quantity 30 tablet<br>• Dosage 75 mg<br>• Per Unit $16.89<br>• Cost $506.67 |
| **Half Life** | 50 hours | 30.8 hours |
| **Drug Interactions** | • A total of 227 drugs are known to interact with Myrbetriq:<br>• 8 major drug interactions (26 brand and generic names)<br>• 93 moderate drug interactions (485 brand and generic names)<br>• 126 minor drug interactions (406 brand and generic names) | • total of 17 drugs are known to interact with Gemtesa:<br>• 17 moderate drug interactions (48 brand and generic names) |
| **Disease Interactions** | • Urinary retention<br>• Hypertension<br>• Liver disease<br>• Renal dysfunction | • Urinary retention |

[53]

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