

# *Drugs for Erectile Dysfunction*

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## **OVERVIEW**

- Erectile dysfunction(ED) and benign prostatic hyperplasia(BPH) are the common urological disorders in male.ED is the inability to maintain penile erection for the successful performance of sexual activity. Cause of ED has many causes but some of them are vascular disease, diabetes, medication, depression and sequelae to prostatic surgery. BPH is nonmalignant enlargement of prostate, which occurs naturally as men age.

## **Drugs used for erectile dysfunction**



- a) Alprostadil<sub>(muse, caverject, edex)</sub>
- b) Avanafil<sub>(stendra)</sub>
- c) Sildenafil<sub>(viagra)</sub>
- d) Tadalafil<sub>(cialis)</sub>
- e) Vardenafil<sub>(levitra, staxyn)</sub>

All the above drugs are phosphodiesterase-5 inhibitors. But

Alporstadil<sub>(muse, caverject, edex)</sub> are synthetic prostaglandin E<sub>1</sub>(PGE<sub>1</sub>) and its mechanism of action is unknown and its available in



## **phosphodiesterase-5 inhibitors**

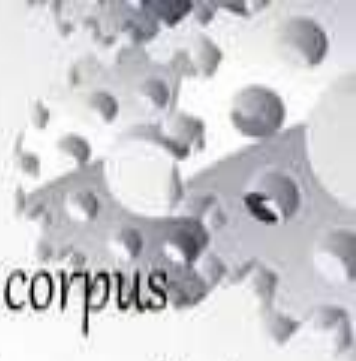
- a) All four PDE5 inhibitors, Avanafil<sub>(stendra)</sub>, sildenafil<sub>(viagra)</sub>, tadalafil<sub>(cialis)</sub>, vardenafil<sub>(levitra, staxyn)</sub> are equally effective in treating of ED and adverse effect profile are similar. However, these agents differ in the duration of action and the effect of food on drug absorption. [Note: sildenafil<sub>(viagra)</sub> and Tadalafil<sub>(cialis)</sub> are also indicated to treat pulmonary hypertension, although the dosage regimen differ for this indication.]

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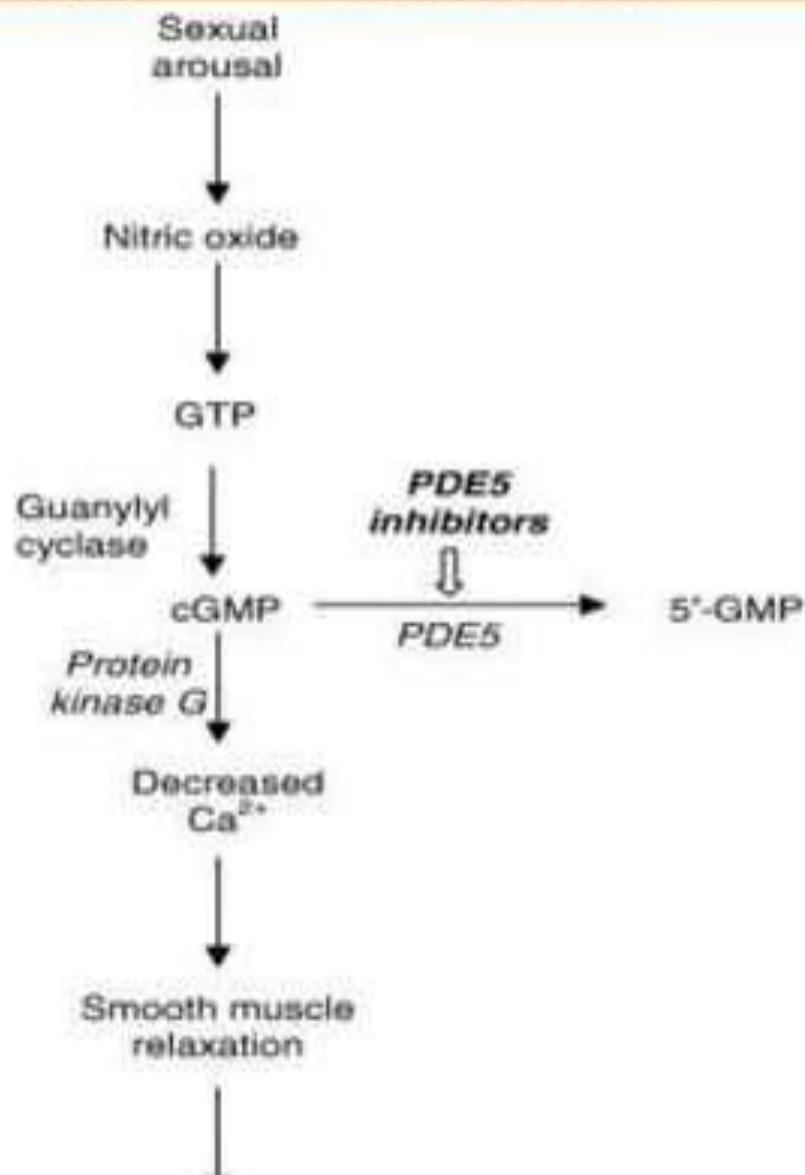
- Taking one of these tablets will not automatically produce an erection. Sexual stimulation is needed first to cause the release of nitric oxide from your penile nerves. These medications amplify that signal, allowing some men to function normally. Oral erectile dysfunction medications are not aphrodisiacs, will not cause excitement and are not needed in men who get normal erection.

## **Mechanism of action**



- Sexual stimulation result in smooth muscle relaxation of the corpus cavernosum (penile tissues), increasing the inflow of blood. The mediator of this response is nitric oxide (NO). NO activates guanylyl cyclase, which form cyclic guanosine monophosphate ( $cGMP$ ) from guanosine triphosphate produced smooth muscle relaxation through a reduction in the intracellular ( $Ca^{2+}$ ) concentration. PDE-5 enzyme responsible for the degradation of ( $cGMP$ ) in the corpus cavernosum. The duration of action of cyclic nucleotide is controlled by the action of phosphodiesterase (PDE).





Schematic diagram illustrating the mechanism of action of the phosphodiesterase type 5 (PDE5) inhibitors. Following sexual arousal, nitric oxide is released from the synapses of neurones in the corpus cavernosum of the penis. This results in accumulation of cyclic guanosine monophosphate (cGMP), produced from Guanosine triphosphate (GTP), which causes smooth muscle relaxation leading to an erection. By preventing cGMP breakdown, PDE5

## Pharmacokinetics

- Sildenafil<sub>(viagra)</sub> and vardenafil<sub>(levitra, staxyn)</sub> have similar pharmacokinetic properties. Both drugs should be taken approximately 1 hour before sexual activity, with erectile enhancement observed for up to 4 hours after administration. Thus the administration of both of drugs must be timed appropriately with regard to anticipated sexual activity. The absorption of both drugs is delayed by consumption of high-fat meal. Tadalafil<sub>(cialis)</sub> has slower onset of action than sildenafil<sub>(viagra)</sub> and vardenafil<sub>(levitra, staxyn)</sub>, but a significantly longer half-life of approximately 18 hours, so its approved for once-daily dosing. The absorption of Tadalafil<sub>(cialis)</sub> is not clinically influenced by food. Avanafil<sub>(stendra)</sub> has the quickest onset of action. It should be taken 30 minutes prior to sexual activity. **All the PDE<sub>5</sub> inhibitors are metabolized by**



## **Advers effects**

- I. The most frequent advers effect of PDE5 inhibitors are headaceh, flushing, dyspepsia and nasal congestion.
- II. Dsiturbances of color vision(loss of bule/green discrimination) may occur with PDE5 inhibitors. Probably because of inhibition of PDE-6(PDE found in the retina that important in color vision).
- III. Tadalafil has been associatd with back pain and myalgias, likely because of inhibition of PDE11(An enzyme found in skeletal muscles).
- IV. PDE5 inhibitors should be used with caution in patients with a history of cardiovasscular disease or those with stornng risk factor of cardiovasscular disease.
- V. PDE5 inhibitors should not be used more than once per day.

## **Alprostadil**



- Alprostadil<sub>(muse, caverject, edex)</sub> are synthetic prostaglandin E<sub>1</sub>(PGE<sub>1</sub>). In penile tissue, PGE<sub>1</sub> allow for relaxation of the smooth muscle in the corpus cavernosum and its mechanism of action is unknown and its available in intraurethral suppository and injectable formulation. Alprostadil<sub>(muse, caverject, edex)</sub> may be used for patients who are not candidate for oral therapies. Alprostadil<sub>(muse, caverject, edex)</sub> acts locally, which may reduce the occurrence of adverse effects.

## **Alprostadil self-injection**



- With this method, you use a fine needle to inject alprostadil (Caverject, Impulse, Edex) into the base or side of your penis. In some cases, medications generally used for other conditions are used for penile injections on their own or in combination. Examples include papaverine, alprostadil and phentolamine. Often these combination medications are known as bimix (if two medications are included) or trimix (if three are included).



## ***Alprostadil urethral suppository***



- Alprostadil<sub>(Muse)</sub> intraurethral therapy involves placing a tiny alprostadil suppository inside your penis in the penile urethra. You use a special applicator to insert the suppository into your penile urethra.

## **Mechanism of Action**

- Alporstadil<sub>(muse, caverject, edex)</sub> causes smooth muscle relaxation by an unknown mechanism of action. It is believed that Alporstadil<sub>(muse, caverject, edex)</sub> increase concentration of cyclic AMP (cAMP) within the cavernosum tissue. As a result, protein kinase is activated, allowing trabecular smooth muscle relaxation and dilation of cavernosal arteries, increase blood flow to the erection chamber, compress venous outflow, so that blood is entrapped and erection may occur.

## ***Pharmacokinetics***

Systemic absorption of Alprostadil (muse, caverject, edex) is minimal, it is quickly metabolized. The onset of action of Alprostadil (muse, caverject, edex) is 5 to 10 minutes when given as urethral suppository and 2 to 25 minutes when administered by injection. The resulting erection may last for 30 to 60 minutes, longer, depending upon the particular patient.



## Advers effects

1. Hypotension or headache is possibility due to PGE<sub>1</sub>-induced vasodilation.
- II. Locally, advers effect of Alporstadil<sub>(muse, caverject, edex)</sub> include penile pain, urethral pain and testicular pain.
- III. Bleeding from the insertion or injection of Alporstadil<sub>(muse, caverject, edex)</sub> is rare.
- IV. Hematoma, ecchymosis and rash are possible from Alporstadil<sub>(muse, caverject, edex)</sub> injection.



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