

Basics of Sexual Dysfunction in Men and Women

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This information is not a recommendation nor is it intended to provide direction regarding diagnoses, treatments, or potential outcomes. Any interpretation of this information is the opinion of Clinic Optimizers and should be used by the prescriber at his/her discretion.

This information (and any accompanying printed material) is not intended to replace the attention or advice of a physician or other health care professional.

Anyone who wishes to embark on any dietary, drug, exercise, or other lifestyle change intended to prevent or treat a specific disease or condition should first consult with and seek clearance from a qualified health care professional.

Erectile Dysfunction (ED) Basics

- ED is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance
- Prevalence increases with age, cardiovascular disease, diabetes mellitus, and hyperlipidemia.
- Diabetes is the most common cause of sexual dysfunction in men. It has been estimated that up to 50-60 % of diabetic men have erectile dysfunction.
- The primary risk factors are smoking, lack of physical exercise and obesity.
- Erectile dysfunction is strongly correlated with depressive symptoms and negatively impacts a man's quality of life.
- The U.S. pharmaceutical industry for treatment of erectile dysfunction is worth over 6 billion dollars

Prevalence of ED

- Prevalence of erectile dysfunction range from 2% to 9% in men between the ages of 40 and 49 years.
- It then increases to 20–40% in men aged 60–69 years.
- In men older than 70 years, prevalence of erectile dysfunction ranges from 50% to 100%.
- Moreover, the worldwide prevalence of erectile dysfunction has been predicted to reach 322 million cases by the year 2025.

Feldman Ha, J Urol 1994; 151:54-61

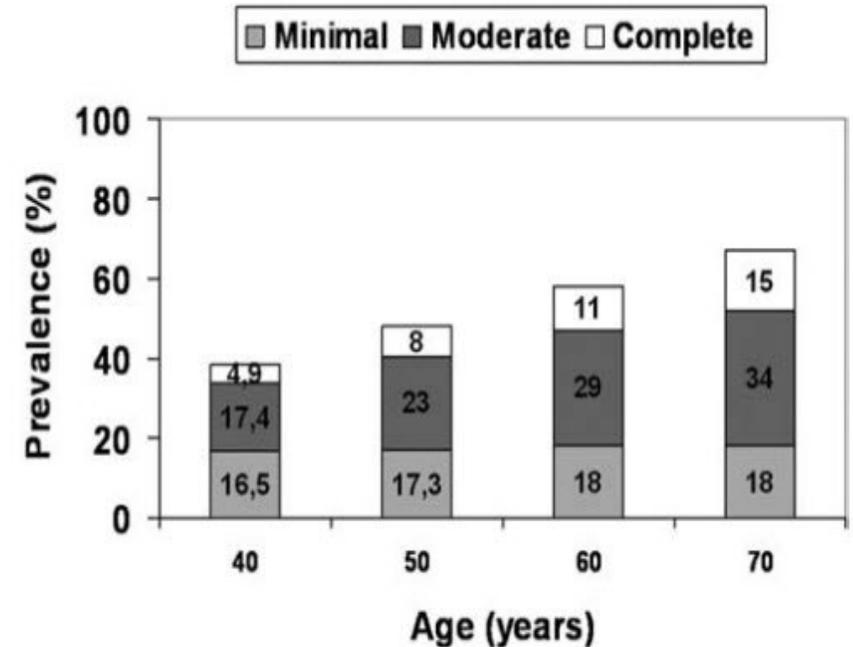


Figure 1. Prevalence and severity of erectile dysfunction in the Massachusetts Male Aging Study.

An Erection Requires a Coordinated Interaction of Multiple Organ Systems

- Psychological
- Hormonal
- Vascular
- Neurologic

Causes of ED

- Organic Causes

- Cardiovascular disease
- Diabetes mellitus
- Surgery on colon, bladder, pelvis, and prostate
- Neurologic causes (lumbar disc, MS, CVA)
- Hormonal deficiency
- Illness

Risk Factors for ED

Massachusetts Male Aging Study¹

- Treated heart disease 39%
- Treated diabetes 28%
- Treated hypertension 15%

¹Feldman Ha, J Urol 1994; 151:54-61

Diabetes-related ED

- About 35 – 75% of men with diabetes will experience at least some degree of ED (impotence) during their lifetime
- Men with diabetes develop ED 10 – 15 years earlier than men without diabetes
 - Often 1st symptom men notice even before they are diagnosed as a diabetic
- Above age of 50, the likelihood of having difficulties with an erection occurs in approximately 50 – 60% of men
- Above the age of 70, there is a 95% likelihood of having some difficulty with erection function

WebMD.com

Causes of ED

- Psychogenic Causes:
 - Anxiety
 - Depression
 - Fatigue
 - Guilt
 - Stress
 - Marital discord
 - Excessive alcohol consumption
 - Amphetamines, opioids, alcohol, and other drugs

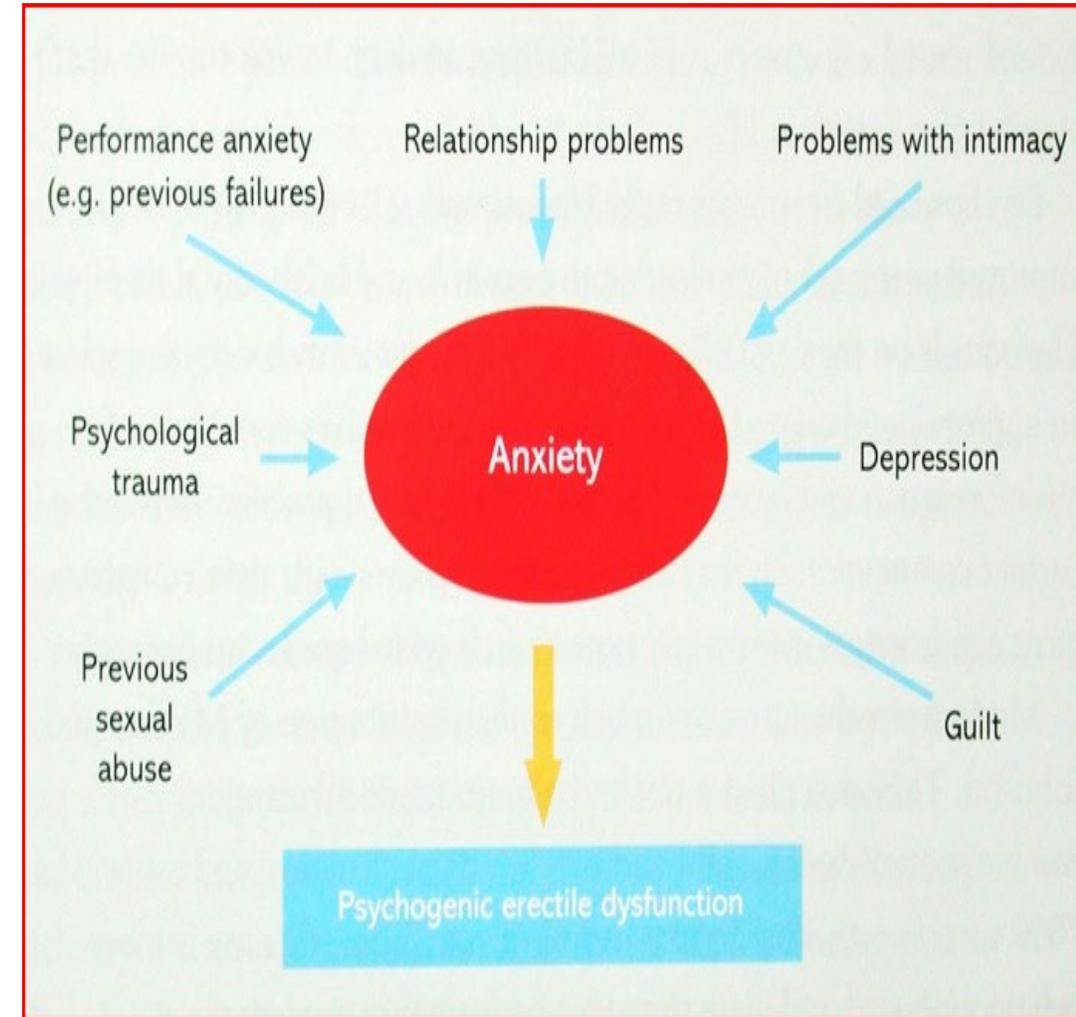
Clues Differentiating Psychogenic From Organic Causes of ED

Psychogenic

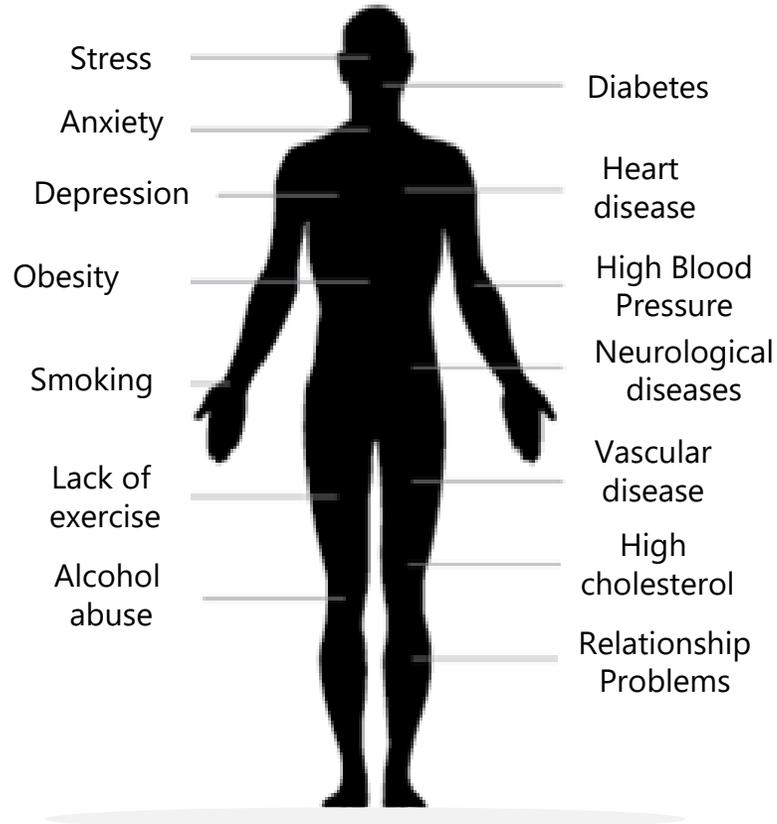
- Sudden onset
- Situational
- Normal waking and nocturnal erections,
- Normal erection with masturbation
- Relationship problems, life event
- Anxiety, fear, depression

Organic

- Gradual onset, All situations
- Reduced or absent waking and nocturnal erections
- No erection with masturbation
- Penile pain.



Causes of Erectile Dysfunction



Risk factors

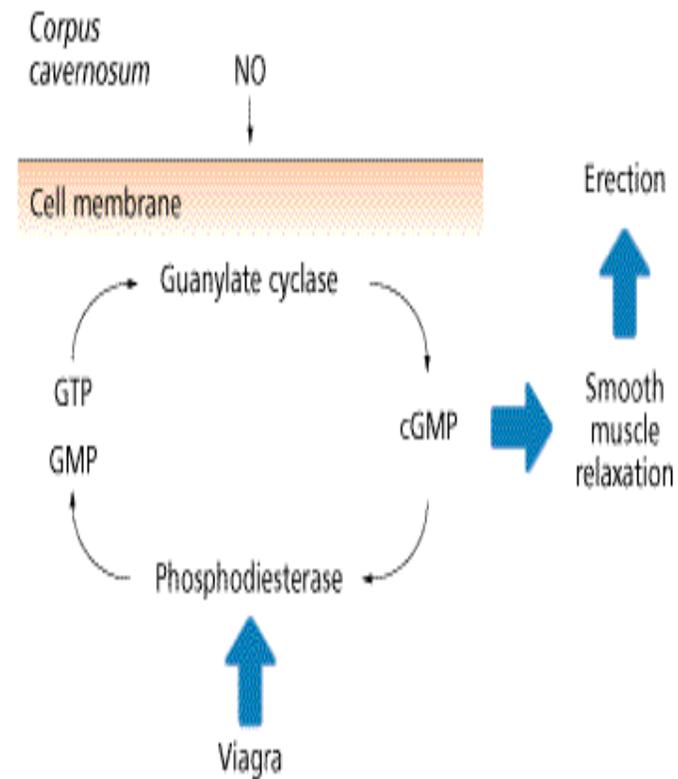
| Risk factors | Examples |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| Aging | |
| Medication | Antihypertensives, antidepressants, digoxin, spironolactone |
| Lifestyle | Smoking, obesity, sedentary lifestyle, alcohol and drug abuse |
| Psychological disorders | Depression, performance anxiety or stress |
| Vascular disorders | Atherosclerosis, ischemic heart disease, peripheral vascular disease |
| Neurological disease | Stroke, multiple sclerosis, spinal cord injury, pelvic trauma or prostate surgery |
| Endocrine abnormalities | Low testosterone, high prolactin |
| Chronic illness | Hypertension, dyslipidemia, diabetes mellitus, cardiovascular disease, chronic renal failure, heart failure, chronic obstructive pulmonary disease |

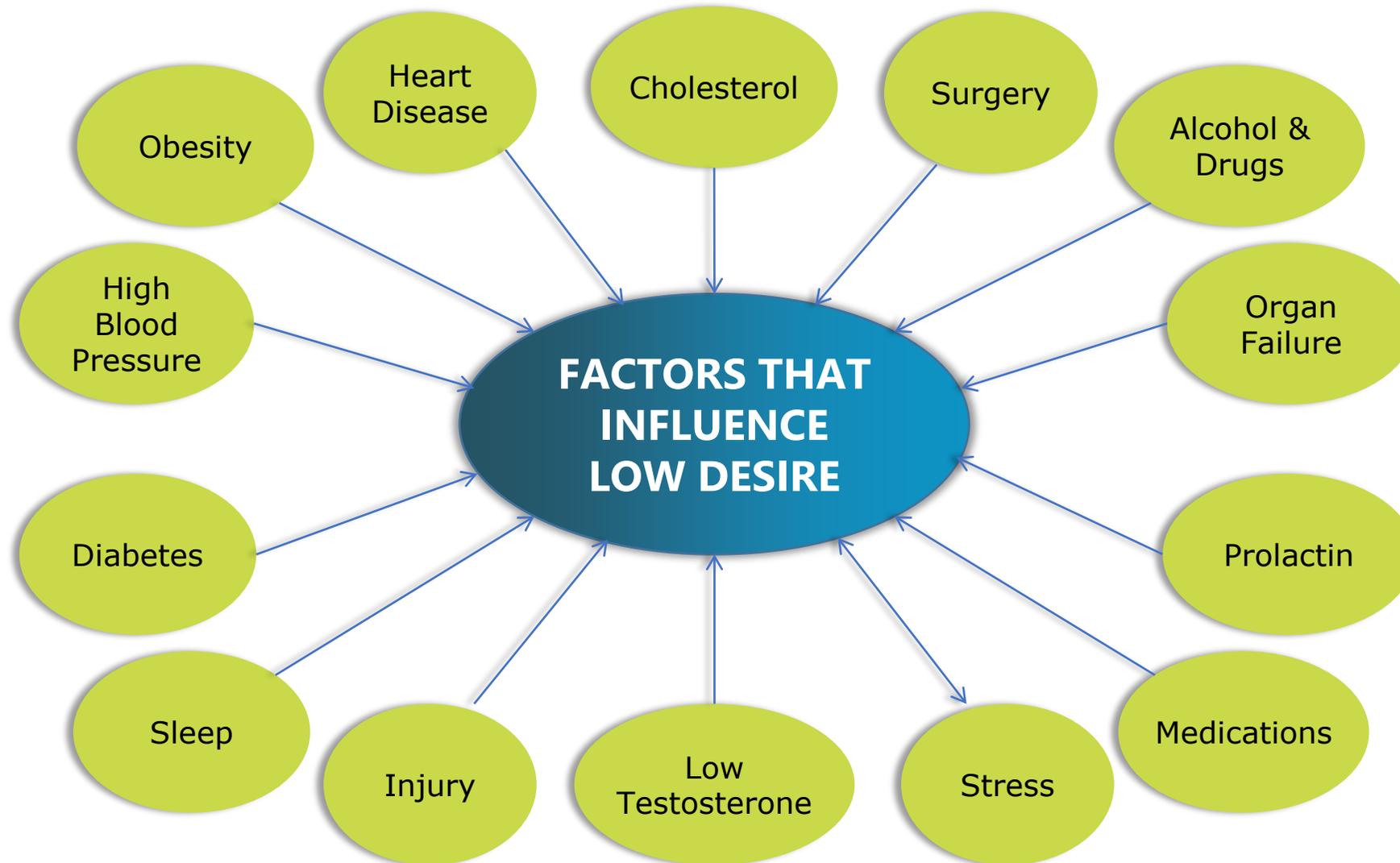
Commonly Used Drugs Associated With Erectile Dysfunction

| Drug Class | Specific drug examples |
|-----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| Beta-blockers Calcium-channel blockers Alpha-adrenergic agonists Cardiac glycosides | propranolol, metoprolol, atenolol verapamil, nifedipine clonidine digoxin |
| Thiazide diuretics Aldosterone antagonists | hydrochlorothiazide spironolactone |
| Fibric acid derivatives | gemfibrozil, clofibrate |
| Selective serotonin reuptake inhibitors Tricyclic antidepressants Other antidepressants | fluoxetine, sertraline, paroxetine, citalopram amitriptyline, desipramine, nortriptyline lithium |
| Benzodiazepines and opiates | lorazepam, alprazolam, diazepam |
| Histamine (H ₂) receptor antagonists | ranitidine, cimetidine |
| Butyrophenones and phenothiazines (antipsychotics) | haloperidol, prochlorperazine, chlorpromazine |
| Hydantoin anticonvulsants | phenytoin |
| Cytotoxic agents | cyclophosphamide, methotrexate |
| Recreational drugs | alcohol, cocaine, marijuana, opiates, meth |

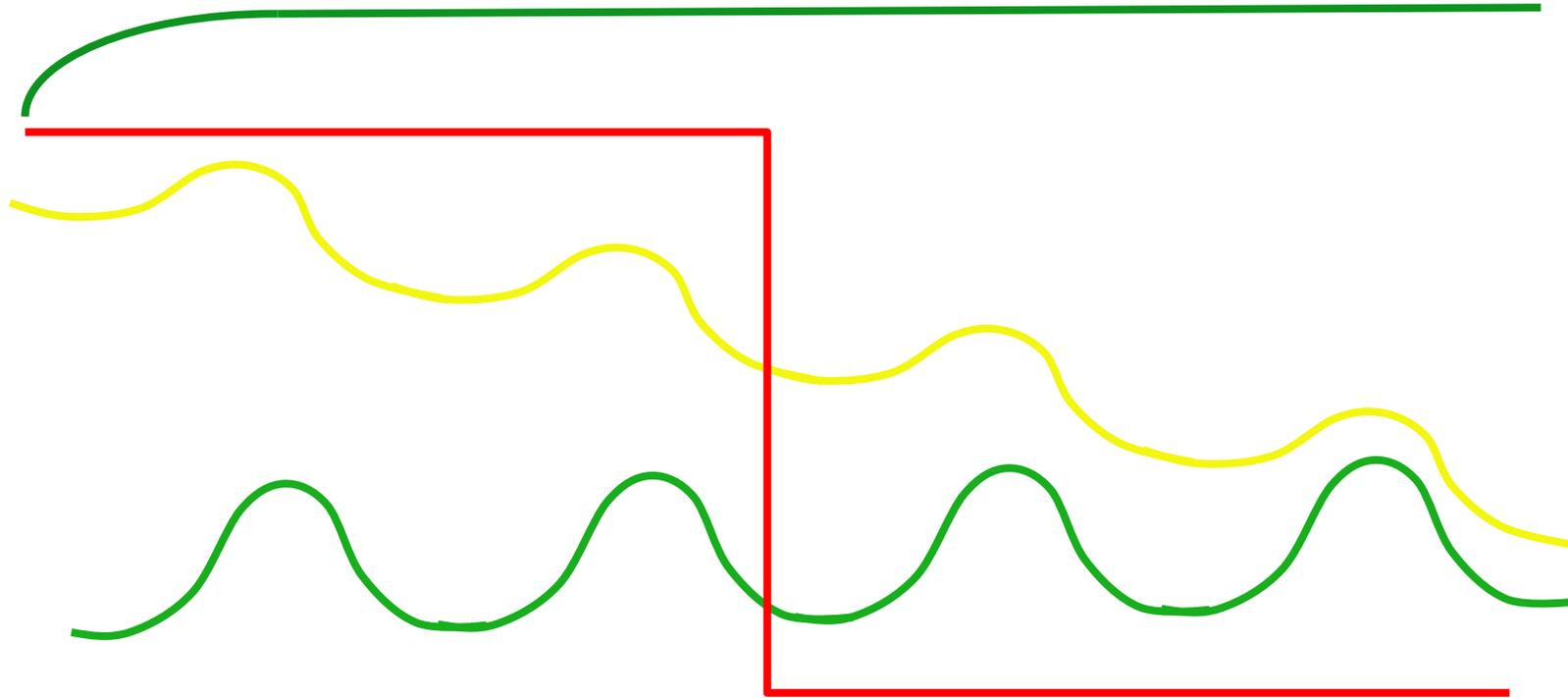
Physiological mechanisms of erections

- Stimulation of penile shaft by the nervous system leads to the secretion of nitric oxide (NO), causing the creation of cyclic guanosine monophosphate (cGMP) which functions to relax blood vessels (vasodilatation) so erectile tissues in the corpus cavernosa can fill with blood, and subsequently cause a penile erection.
- Phosphodiesterase type 5 (PDE5) is always present in the penis and functions to destroy cyclic GMP, causing vasoconstriction of erectile tissues and resulting in the loss of erection. In normal males, the loss of an erection occurs after orgasm and ejaculation of sperm.





Evaluating Libido



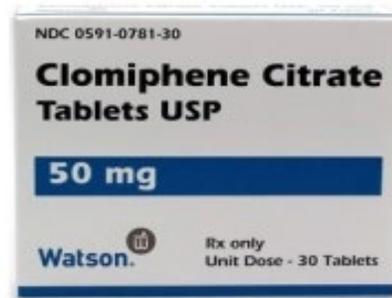
History of Treatment for Erectile Dysfunction

- 1930s: Dr. John R. Brinkley experimented with goat glans to treat impotence
- 1948: Masters and Johnson published the book Sexual Behavior in the Human Male and five years later when they published Sexual Behavior in the Human Female.
- Up until the 1970's it was generally believed that the majority of ED was psychological in nature and that the mind must be treated and the sexual situation counseled in order to treat and effectively cure the problem. But penile vacuum pumps were also used to erect the penis by drawing blood into the penile tissue.
- 1973: American Medical Devices developed inflatable prosthetic devices
- 1980: Intracorporal injections developed such as alprostadil
- Early 90's an herbal supplement, Yohimbine created but advised against
- 1999: Pfizer introduced VIAGRA (sildenafil)
- 2000: TAP Pharmaceutical Products, developed the first oral centrally acting drug: Apomorphine HCL, marketed under the brand name Uprima
- 1999-2003: Vardenafil and tadalafil entered the market

ED Treatment Options

- Oral medications – Phosphodiesterase Type 5 Inhibitors (PDE-5): Viagra (sildenafil), Levitra (vardenafil), Cialis (tadalafil), and Stendra (avanafil).
- Urethral suppositories (MUSE)
- Injection therapy - Caverject, Trimix, Bimix, Quadmix
- Vacuum constriction device
- Surgery (implant)
- Sex therapy

TRT-RELATED COMPOUNDED PRODUCTS



Compounded Treatment for Sexual Dysfunction



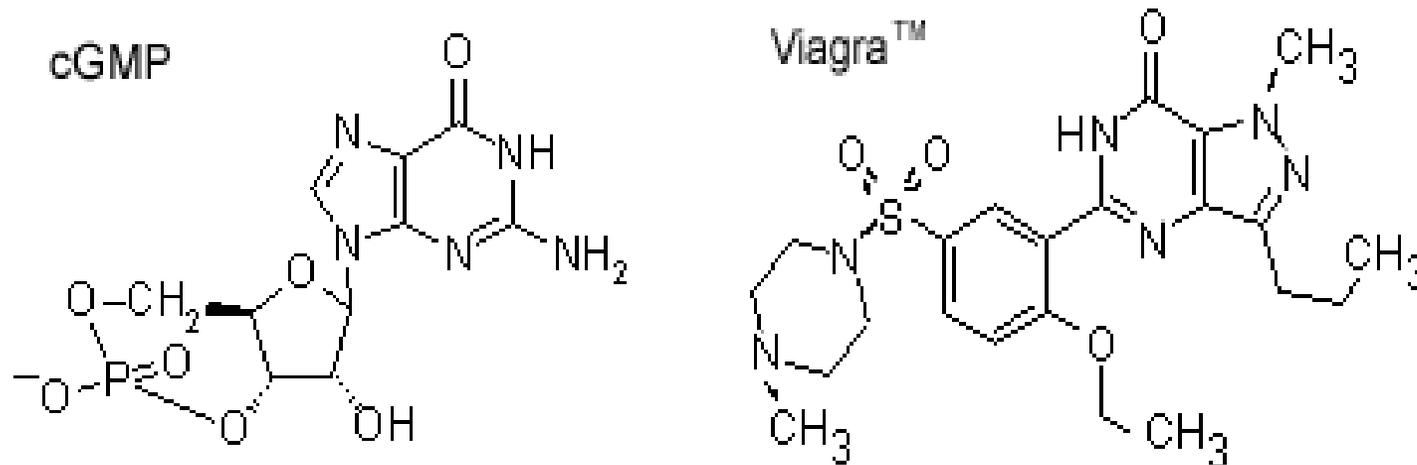
PED5 Inhibitor Basics



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The discovery of Viagra

- Pfizer accidentally fell upon Viagra as a treatment of erectile dysfunction. They were initially searching for a vasodilator to treat angina pectoris.
- Their goal was to find a molecule that would bind to PDE's active site, so that it wouldn't be able to convert cGMP to the inactive GMP form. They studied the structure of the substrate cGMP .
- Compare cGMP and Viagra



What is a PDE5 Inhibitor?

- **PDE-5 inhibitor**, in full **phosphodiesterase-5 inhibitor**, category of drugs that relieve erectile dysfunction in men.
- PDE-5 inhibitors work by blocking, or inhibiting, the action of phosphodiesterase-5 (PDE-5), an enzyme naturally present in the corpus cavernosum, the spongy erectile tissue of the penis.
- Under normal circumstances, sexual arousal in the male stimulates neurons in the corpus cavernosum to release nitric oxide, a chemical compound that causes the formation of cyclic guanosine monophosphate (cGMP); cGMP in turn causes the smooth muscle of the corpus cavernosum to relax, allowing blood to flow into the penis and produce an erection.
- PDE-5 breaks down cGMP, and so the PDE-5 inhibitors, by blocking the action of the enzyme, maintain higher levels of cGMP and preserve a satisfactory erection



PDE5 Commercial Indications

Comparison of Currently FDA Approved PDE-5 Inhibitors

- **PDE-5 Indications:** Sildenafil, vardenafil, tadalafil, and avanafil are approved for as-needed use in the treatment of ED.
- In 2008, tadalafil was granted FDA approval for once-daily use in the treatment of ED and in 2011, it was given an indication for BPH with or without ED.
- Sildenafil and tadalafil are also approved for PAH under the trade names of Revatio and Adcirca, respectively.

| Medication | Viagra (sildenafil) | Levitra (vardenafil) | Cialis (tadalafil) | Stendra (avanafil) |
|--------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Type | PDE-5 Inhibitor | PDE-5 Inhibitor | PDE-5 Inhibitor | PDE-5 Inhibitor |
| Dose | 25-100mg | 5-20mg | 5-20mg | 50-200mg |
| Peak Time | 1 hour | 42-54 minutes | 2 hours | 15-30 minutes |
| Gone From Body | 8-12 hours | 8-12 hours | 36 hours | 8-12 hours |
| Contra-indicated | Nitrates | Nitrates | Nitrates | Nitrates |
| FDA Approval | 3/29/98 | 8/20/03 | 2/02/04 | 4/1/12 |
| Effects of eating and drinking | No food or drink 1-2 hours before | Not effected by food or alcohol | Not effected by food or alcohol | Not effected by food or alcohol |
| Side Effects | Headache, flushing, nasal congestion, abnormal vision, heartburn, bloodshot eyes | Headache, flushing, nasal congestion, abnormal vision, heartburn, bloodshot eyes | Headache, flushing, nasal congestion, heartburn, bloodshot eyes, backache, leg cramps | Headache, flushing, nasal congestion, heartburn, bloodshot eyes, backache, leg cramps |
| Other | For many patients the most potent. Negatives are shorter half-life (than Cialis), less effective when taken with fatty meal. Most side effects. | Greater selectivity (and thus usually fewer side effects) than Viagra. Slower to take effect when taken with fatty meal. | Greater selectivity (and thus usually fewer side effects) than Viagra. | Greater selectivity (and thus usually fewer side effects) than Viagra. Slower to take effect when taken with fatty meal. |

Source: Smith et al. The devil is in the details: an analysis of the subtleties between phosphodiesterase inhibitors for erectile dysfunction. *Transl Androl Urol.* 2016 Apr; 5(2):181-186.



ED Medication Profiles

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Pharmacy Price PDE5 Inhibitors

| Drug | Strength | Quantity | Price |
|-----------------|----------|----------|----------------------|
| Viagra®/Generic | 100mg | 4 | \$54.83/\$44.83 |
| Levitra® | 20mg | 4 | \$73.43 |
| Cialis® | 20mg | 4 | \$78.32 |
| Cialis® | 5mg | 28 | \$146.50 (\$20.93/4) |

Benefits of Compounded PDE5i Orally Disintegrating Tablets (ODT)

- **Unique Dosage Form-** Empower's Orally Disintegrating Tablets (ODT'S) offer patients an option to administer the medication without needing water. This is a huge benefit for patients who have trouble swallowing pills or do not have immediate access to water in order to take the medication.
- **ODTs** are elegant pressed tablets that can be taken orally with easy chewing or sublingually/buccally when dissolved under the tongue or between the cheek and gum. sublingual/buccal administration may possible faster onset of action and reduce 'upset stomach.'
- **Empower's ODT's are Quad Scored** which allows providers dosing flexibility for each individual patient.
- **Unique Strength-** Empower's ODT's come in unique strengths that are not commercially but are necessary to treat each individual patients.



ODT Formulation Highlights

- Affordable
- Possible faster onset of action*
- Reduce upset stomach*
- Quad-scored
- Individually perforated blister packs (10/pk)
- Will not melt in transit
- No artificial dyes



ODT Product Details

- The price for ODTs is significantly **less expensive** than our troches
- ODTs are elegant pressed tablets that can be taken orally with easy chewing or sublingually/buccally when dissolved under the tongue or between the cheek and gum. sublingual/buccal administration may possible faster onset of action and reduce 'upset stomach.'
- ODTs **dissolve faster** than troches (under 45-60 seconds)
- Unlike troches, ODTs can dissolve in the mouth without **additional water**
- All ODTs are **quad-scored** so that they can be broken into smaller dosage forms (ie take 1/4 of a 25mg tadalafil ODT)
- Empower's ODTs will be dispensed in **individually perforated blister packs** to allow safe and discreet transport
- ODTs do not melt and can be shipped via ground
- ODTs are hard enough that they will not break in transit, but still have a rapid dissolution speed (ability to dissolve sublingually within 45-60 seconds)
- ODTs are compounded utilizing an automated pharmaceutical tablet press
- ODTs have passed potency testing at a third-party analytical lab
- Each batch of ODTs 100% check weighed to ensure quality





NEW PRODUCT ANNOUNCEMENTS

Orally Disintegrating Tablets

Empower Pharmacy is pleased to announce the release of PDE-5 inhibitors in Oral Disintegrating Tablet (ODT) dosage form. Empower Pharmacy's ODTs have a rapid dissolution speed (ability to dissolve sublingually within 60 seconds) and a possible faster onset of action.

PDE-5 inhibitor ODTs highlights:

- Elegant pressed tablets compounded utilizing pharmaceutical tablet press
- Dispensed in individually perforated blister packs to allow safe and discreet transport
- ODTs have passed potency testing at a third-party analytical lab
- Each batch of ODTs 100% check weighed to ensure quality

Benefits of ODTs:

- Less expensive than troches
- Can dissolve without water
- Possible faster onset of action
- Reduces "upset stomach" sometimes experienced with oral tablets
- Quad-scored for dosing flexibility
- No artificial dyes
- Do not melt in transit, can be shipped UPS Ground



*Note: All ODTs we produce are white

[Click here for the ODT powerpoint with additional info](#)

Product Inventory

Available NOW:

Sildenafil ODT 125 mg

Tadalafil ODT 25 mg

Vardenafil ODT 25 mg

Coming Soon:

Avanafil ODT 250 mg



NOTE: Once all PDE5i products have been released as an ODT, we will be completely discontinuing PDE5i troches and capsules over a gradual timeline



Cost per 10 pack

All ODTs have the **same pricing** regardless of drug name/strength depending on tier and patient pricing

| Product Name | Strength | Patient Price | Tier 3 | Tier 2 | Tier 1 |
|----------------|----------|---------------|--------|--------|--------|
| Sildenafil ODT | 125 mg | \$55 | \$52 | \$46 | \$37 |
| Tadalafil ODT | 25 mg | \$55 | \$52 | \$46 | \$37 |
| Avanafil ODT | 250 mg | \$55 | \$52 | \$46 | \$37 |
| Vardenafil ODT | 25 mg | \$55 | \$52 | \$46 | \$37 |



Cost per Dose

| Product Name | 1 Tablet | $\frac{3}{4}$ Tablet | $\frac{1}{2}$ Tablet | $\frac{1}{4}$ Tablet |
|----------------|----------|----------------------|----------------------|----------------------|
| Sildenafil ODT | 125 mg | 93.75 mg | 62.5 mg | 31.25 mg |
| Tadalafil ODT | 25 mg | 18.75 mg | 12.5 mg | 6.25 mg |
| Avanafil ODT | 250 mg | 187.5 mg | 125 mg | 62.5 mg |
| Vardenafil ODT | 25 mg | 18.75 mg | 12.5 mg | 6.25 mg |

| | | | | |
|-----------------------|--------|--------|--------|--------|
| Patient Price per ODT | \$5.50 | \$4.13 | \$2.75 | \$1.38 |
|-----------------------|--------|--------|--------|--------|



Labeling

- Blister packets
- 3 sheets (30 ODT total) per envelope
 - Fillers will be used for orders less than 30
- Front: Empower Logo, Medication name, LOT #
- Back: Prescription Label



Prescription Requirements

| Not Acceptable | Acceptable |
|----------------|-------------------------|
| ODT/Troche | ODT |
| Oral Tablet | Dissolving Tablet |
| Tablet | Rapid Dissolving Tablet |
| | Meltaway |



PDE5 Inhibitor Contraindications

Since PDE5 inhibitors such as sildenafil, tadalafil, and vardenafil may cause transiently low blood pressure (hypotension), organic nitrates should not be taken for at least 48 hours after taking the last dose of tadalafil. Using organic nitrates within this timeframe may increase the risk of life-threatening hypotension.

PED5 Inhibitor Contraindications

Contraindications:

- Organic Nitrites:
 - Oral
 - Sublingual
- Severe cardiac disease
 - Obtain stress testing
- Careful with Norvir since it boosts PDE blood levels

Compounded PDE-5 Inhibitors

- Compounded less than 1/5th the cost of brand name
- Made from the same raw materials sourced from FDA approved suppliers
- Must be a different strength and/or dosage form than commercially available
- \$5 to \$6 per dosage (compared to \$40-\$60 per tablet)
 - Sildenafil 110mg capsule
 - Tadalafil 25mg capsule
 - Avanafil 200mg troche
 - Vardenafil 20mg troche
 - ODT formulations now available

PDE5 Inhibitors Contraindications

Contraindications:

- Organic Nitrites:
 - Oral
 - Sublingual
- Severe cardiac disease
 - Obtain stress testing
- Careful with Norvir (HIV drug) since it boosts PDE blood levels

Penile Injection Therapies



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Penile Injection Therapy

Caverject, Edex, Bi/Tri/Quad-Mix

- Mechanism of action: smooth muscle vasodilator
- Monotherapy (prostaglandin E1) or combination of 2 or 3 agents (Papaverine+ Phentolamine + Alprostadil)
- Administration: 10, 20, 40ug
- Inject directly into corporeal bodies of the penis
- Results: 70%-90%
- Dropout rates: 25%-60%
- Side effects: pain (36%), priapism (4%), fibrosis

Intracavernosal Penile Injections



- Tri-Mix is a mixture of Papaverine, Phentolamine, and Prostaglandin
- Only offered by compounding pharmacies
- More effective in smaller doses than if these compounds were used individually
- 503B Outsourcing Facilities who specialize in ED offer numerous strengths and combinations that include a prostadil
- Lyophilized version preferred for longer shelf-life (lower cost to the patient)



Penile Injection Therapy

- Smooth muscle – relaxing medication injected directly into the penis
- Insulin needle and syringe
- Drug dosage - .5 cc or less
- 5-15 minute response time
- 30 minute to 2 hour duration

- Possible side effects
 - Pain on administration
 - Prolonged erections
 - Hematomas
 - Scarring

Intracavernosal Penile Injections

- Tri-Mix is a mixture of Papaverine, Phentolamine, and Prostaglandin
- Only offered by compounding pharmacies
- More effective in smaller doses than if these compounds were used individually
- 503B Outsourcing Facilities who specialize in ED offer numerous strengths and combinations that include aprostadil
- Lyophilized version preferred for longer shelf-life (lower cost to the patient)



Multiple strength combinations of ICP Injections are available:

Bi-Mix 5 mL vial. Papaverine HCl 30mg/mL, Phentolamine Mesylate 1mg/mL

Super Bi-Mix: 5 mL vial. Papaverine HCl 30mg/mL, Phentolamine Mesylate 2mg/mL

Tri-Mix: 5 mL vial. Papaverine 30mg/mL, Phentolamine Mesylate 1mg/mL, Prostaglandin E1 10mcg/mL

Super Tri-Mix: 5 mL vial. Papaverine 30mg/mL, Phentolamine Mesylate 2mg/mL, Prostaglandin E1 20mcg/mL

Quad-Mix: 5 mL vial. Papaverine HCl 30mg/mL, Phentolamine Mesylate 2mg/mL, Prostaglandin E1 20mcg/mL, Atropine Sulfate 200mcg/mL

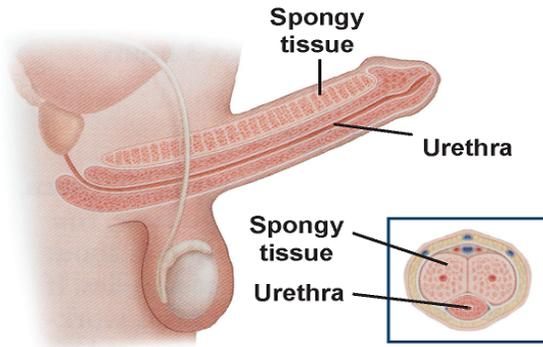
Super Quadmix: 5 mL vial. Papaverine HCl 30mg/mL, Phentolamine Mesylate 4mg/mL, Prostaglandin E1 40mcg/mL, Atropine Sulfate 400mcg/mL

Priapism Rx: 2mL pre-diluted Phenylephrine HCl 0.1% (1mg/mL) vials.

Starting dose: Injection of 0.05-.3 cc of reconstituted Tri-Mix, Super Tri-Mix or Quad-Mix solution (29-30 gauge ½ inch) as needed before sexual activity. Priapism rescue: If erection lasts more than 3 hours, inject phenylephrine at 0.5mL every 5 minutes up to 2mL until detumescence (soft penis) start occurring

Anatomy of an Erection

To produce an erection, the brain, nerves, blood vessels, and hormones all have to work together. The result is extra blood flowing into the penis and staying there until after orgasm (climax). The penis is made up of spongy tissue filled with blood vessels. When stimulated, the blood vessels relax and expand. This brings more blood to the penis. The tissue swells and becomes firm enough for sex.



When There's a Problem

If the blood vessels don't expand, extra blood can't go to the tissue, so the penis stays soft. This problem is called erectile dysfunction (ED). It can make intercourse frustrating or even impossible. Emotional issues can lead to ED, but the cause is often physical. Common causes include other health problems and side effects of medications.

Injections Can Help

Medications used for self injection relax penile blood vessels. Blood can then flow freely into the penis and cause an erection. Steps for self injection are described inside this brochure.

A Satisfying Sex Life

Penile self-injection is a simple technique. But it may cause a major change in your sex life. Some men even find that self injection leads to an increase in natural erections. If you have questions or concerns about self-injection or ED, talk to your healthcare provider.



PENILE SELF-INJECTION

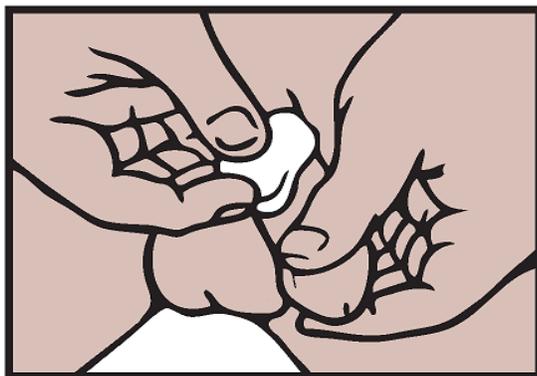


Treatment For Erectile Dysfunction

Sample Steps to Erection

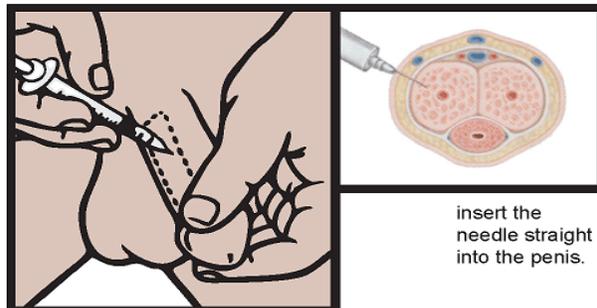
Self injection is a good option for many men with erectile dysfunction (ED). A tiny needle is used to inject medication into the penis. This helps your penis become hard and stay that way long enough for sex. Sex and orgasm will feel as good as always. You may be nervous about doing self injection at first, but with practice it will get easier. Your healthcare provider will show you how to do self injection the first time. The simple steps are outlined in this brochure.

Preparing for Injection



1. Wash your hands well with soap and water.
2. Prepare the medication (if needed).
3. Sit or stand in a comfortable position in a warm, well-lit room. If you need to, sit or stand in front of a mirror.
4. Find an injection site on one side of your penis, in a place with no visible veins. (Don't inject into the top, bottom, or head of the penis.)
5. Clean the injection site with an alcohol swab. Grasp the head of your penis firmly with your thumb and forefinger (don't just pinch the skin). Stretch the penis so the skin on the shaft is taut.

Injecting the Medication



The injection site can be any part of the shaded area

1. Rest your penis against your inner thigh and pull it gently toward your knee. Don't twist or rotate it. This way you'll be sure to inject the medication into the spot you chose and cleaned before.
2. Hold the syringe between your thumb and fingers, like you're holding a pen. Rest your forearm on your thigh for support.
3. Insert the needle at a 90-degree angle with the shaft near the base of the penis. Do this quickly to reduce discomfort. (The needle should go in easily. If it doesn't, stop right away)
4. Move your thumb to the plunger. Press down to inject the medication, counting to 5.
5. Remove the needle and dispose of it safely.

Gaining an Erection

1. Apply pressure to the injection site for a few minutes. This prevents swelling and bruising and helps spread the medication.
2. Stand up. This may help your erection develop. Foreplay often helps, too.
3. Your penis should become firm within 10 to 20 minutes. The erection will last long enough for sex, and maybe longer.

Notes About Self-Injection

- You may feel a mild burning during injection. This is okay. But if you feel pressure or severe pain, stop the injection. There may be a problem with the injection site.
- Only inject the medication on the side of your penis. It may not work if injected elsewhere.
- To prevent scarring, inject in a different spot each time.
- Don't use this treatment if you have a bleeding disorder or any risk of infection.
- Get medical help right away if your erection lasts longer than 2 to 3 hours.

Work with Your Doctor

Ask how often you can safely repeat injections, as well as any other questions you have. You and your healthcare provider will talk about follow up exams and how to get supplies. If the medication doesn't work or stops working over time, tell your healthcare provider.



Call Your Doctor If You Have:

- An erection that lasts longer than 2 to 3 hours
- Bleeding or bruising
- Severe pain
- Scarring or curvature of the penis



Priapism Treatment

BD Inject-Ease



Will inject needle into the skin but you still need to push the plunger to dispense injection

\$45.00

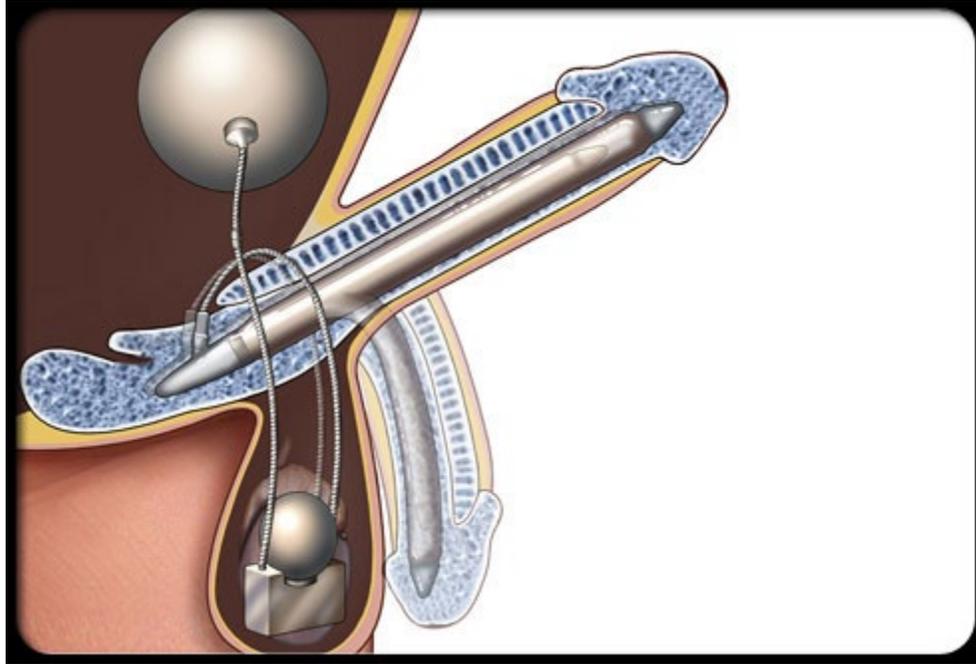
Autoject 2



Does a complete injection

\$69.95

Other Options for ED



Penile Prosthesis

Vacuum Constriction Devices



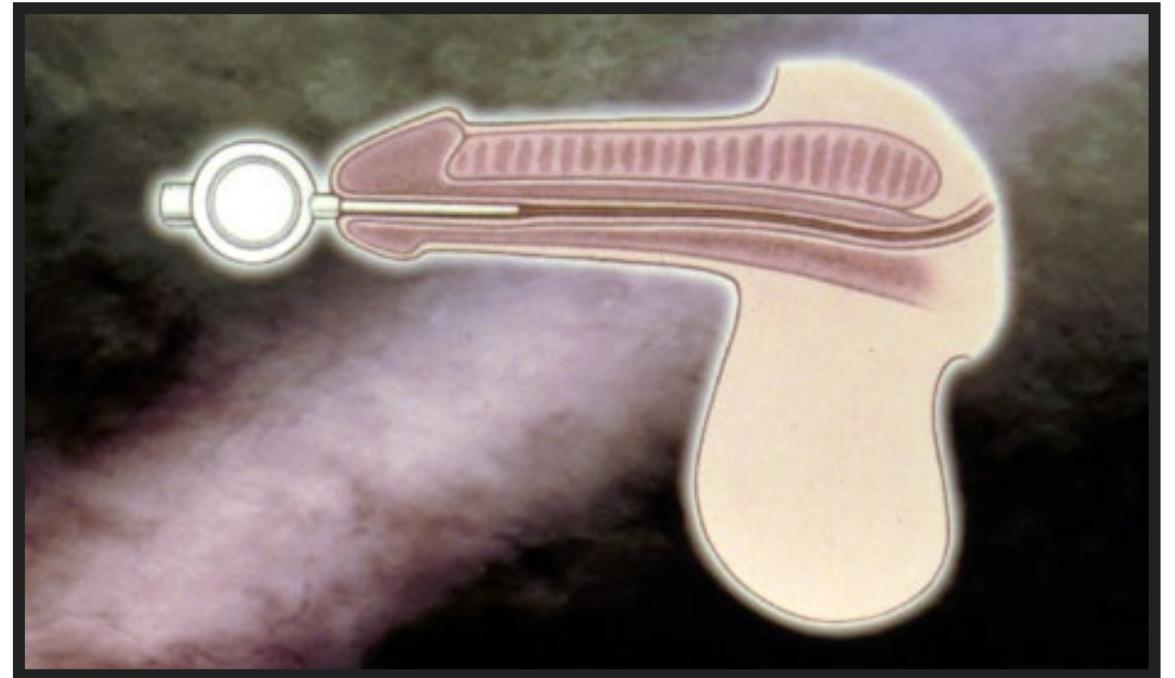
Alprostadil Brand Names

- Caverject: Direct injection of papaverine/alprostadil.
- MUSE: alprostadil is produced in intraurethral pellets; tiny tablets that can be inserted down into the opening of the penis with the aid of a minute insertion stick.
- “TriMix”: prostaglandin E1 (PGE1), papaverine/phentolamine

Caverject



Transurethral Medication: MUSE



ED Rx Price Comparison

| Medication | Cost Per Dose |
|-------------------------------|-----------------|
| Viagra 100mg/Generic | \$13.70/\$11.20 |
| MUSE 1000µg | \$48.53 |
| Intraurethral Gel 250/0.3/0.2 | \$24.98*** |
| Caverject 20ug | \$40.56* |
| Tri-Mix | \$3.94** |

*Caverject is a single use vial so product. Manufacturer recommends once mixed product to be discarded regardless what dose is used

** Tri-Mix dose used here is 40 units (0.4ml). In a 10ml vial a person would get 24 doses

***Need to order 6 doses to get this price

Basics of Female Sexual Dysfunction



This information is not a recommendation nor is it intended to provide direction regarding diagnoses, treatments, or potential outcomes. Any interpretation of this information is the opinion of Clinic Optimizers and should be used by the prescriber at his/her discretion.

Female Sexual Dysfunction

- 43% of American women suffer from sexual dysfunction. (over 50 million American women)
Highest proportion occurs between the ages of 18 and 29.
- Many women can reach orgasm when the clitoris is stimulated, but only about half of women regularly reach orgasm during sexual intercourse. About 1 of 10 women never reaches orgasm.
- The World Health Organization International Classifications of Diseases has divided Female Sexual Dysfunction into four disorders:
 - (1) Desire disorder: a persistent absence of desire for sexual activity.
 - (2) Arousal disorder: a persistent inability to attain or maintain sufficient sexual excitement.
 - (3) Orgasm disorder, a persistent difficulty, delay or absence of orgasm after sufficient stimulation.
 - (4) Pain disorder, persistent genital pain associated with sexual intercourse or stimulation.

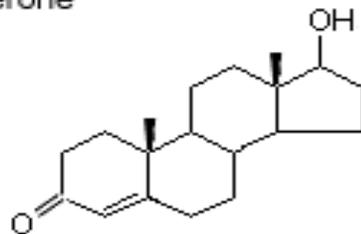
Causes of Female Sexual Dysfunction

- Arousal and orgasmic disorders can be caused by a lack of blood circulation to the clitoris and genital area and may be related to medical conditions such as:
 - Menopause
 - Vascular disease
 - High blood pressure
 - Diabetes
 - Pelvic trauma
 - Other conditions related to poor blood flow
- Fluctuations in the levels of estrogen and testosterone hormones, which occur monthly and during pregnancy, can affect sex drive.
- In postmenopausal women, sex drive may be reduced because estrogen levels decrease. Sex drive may also be reduced in women who have had both ovaries removed.
- A reduction in sex drive may result from depression, anxiety, stress, or problems in a relationship. Use of certain drugs, including anticonvulsants, chemotherapy drugs, beta blockers (antihypertensive Drugs), and oral contraceptives, can also reduce the sex drive. So can drinking excessive amounts of alcohol.
- Women who have undergone treatment for breast or ovarian cancer are at high risk for sexual dysfunction.

Testosterone for FSD

- Most commonly used drug for treatment of FSD, especially in post-menopausal women.
- Works to stimulate sexual desire.
- Extremely low doses required- 20mg administered subcutaneously every 1-2 weeks.
- Creams and pellets, and combinations with estrogen and progesterone are compounded.
- Side effects: masculinization and menstrual issues at higher doses.
- Compounding pharmacies are the only source of transdermal or pellet testosterone for women.

testosterone



Signs and Symptoms of Testosterone Deficiency in Women

Signs

- Decreased lean body mass
- Increased body fat
- Thinning or loss of hair
- Osteopenia or Osteoporosis

Symptoms

- Decline in sexual motivation or libido
- Fatigue and lack of energy
- Lack of sense of well being
- Lack of concentration
- Orgasmic dysfunction
- Arousal disorder
- Depression

Viagra (sildenafil) for Women

- Due to Viagra's PDE5 inhibition it may improve vaginal/clitoral engorgement and lubrication.
- 84 percent success rate of decreasing symptoms of female sexual dysfunction, but it doesn't have FDA approval yet.

Reference: *Faubion, S. et al. Mayo Clinic, Am Fam Physician. 2015 Aug 15;92(4):281-288*

Vaginal Atrophy

- A decrease of 50% of the blood flow to the vulva after menopause can be restored by estrogen therapy
- Regular intercourse also maintains youthful vulvovaginal tissue
- Other products including SERMs (ospemifene) and DHEA may also alleviate vaginal atrophy

Medications Associated with Female Sexual Dysfunction

| Medications Associated with Female Sexual Dysfunction | | | |
|-------------------------------------------------------|-----------------|-------------------|------------------|
| TYPE OF DYSFUNCTION | | | |
| MEDICATION | DESIRE DISORDER | AROUSAL DISORDERS | ORGASM DISORDERS |
| Amphetamines and related anorectic medications | | | + |
| Anticholinergics | | + | |
| Antihistamines | | + | |
| Cardiovascular and antihypertensive medications | | | |
| Antilipids | + | | |
| Beta blockers | + | | |
| Clonidine | + | + | |
| Digoxin | + | | + |
| Methyldopa | + | | |
| Spironolactone | + | | |
| Hormonal preparations | | | |
| Antiandrogens | + | + | + |
| Danazol | + | | |
| Gonadotropin-releasing hormone agonists | + | | |
| Gonadotropin-releasing hormone analogues | + | + | |
| Hormonal contraceptives | + | | |

| | | | |
|----------------------------------------------------------|---|---|---|
| Tamoxifen | + | + | |
| Ultra-low-potency contraceptives | + | + | |
| Narcotics | | | + |
| Psychotropics | | | |
| Antipsychotics | + | | + |
| Barbiturates | + | + | + |
| Benzodiazepines | + | + | |
| Lithium | + | + | + |
| Monoamine oxidase inhibitors | | | |
| Selective serotonin reuptake inhibitors | + | + | + |
| Trazodone | + | | |
| Tricyclic antidepressants | + | + | + |
| Venlafaxine | + | | |
| Other | | | |
| Aromatase inhibitors | + | + | |
| Chemotherapeutic agents | + | + | |
| Histamine H ₂ blockers and promotility agents | + | | |

Reference: *Faubion, S. et al. Mayo Clinic, Am Fam Physician. 2015 Aug 15;92(4):281-288*

Treatments for Sexual Dysfunction in Women

Dyspareunia: Painful sex

Reference:

Faubion, S. et al. Mayo Clinic, Am Fam Physician. 2015 Aug 15;92(4):281-288.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

| CLINICAL RECOMMENDATION | EVIDENCE RATING | REFERENCES |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|--------------------------------------------------------------|
| Bupropion (Wellbutrin) in higher dosages (150 mg twice daily) has been shown to be effective as an adjunct for antidepressant-induced sexual dysfunction in women. | B | 17 |
| Sildenafil (Viagra) may benefit women with sexual dysfunction induced by selective serotonin reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor use. | B | 18 |
| Female genital sexual pain disorders are complex and most effectively managed with a comprehensive, multidisciplinary approach that addresses contributing biopsychosocial factors. | C | 19 |
| Group cognitive behavior therapy has been shown to effectively treat low sexual desire. | C | 7 |
| Mindfulness-based interventions have been shown to effectively treat low sexual desire and arousal, and acquired anorgasmia. | B | 7 , 25 , 26 |
| Directed masturbation is recommended for lifelong anorgasmia. | A [corrected] | 27–29 |
| Local vaginal estrogen therapy is recommended and preferred over systemic estrogen therapy for treatment of genitourinary syndrome of menopause and related dyspareunia when vaginal dryness is the primary concern. Because of potential adverse effects, the use of estrogens, especially systemic estrogens, should be limited to the shortest duration compatible with treatment goals. | A | 14 , 21 , 31 |
| Ospemifene (Osphena) is modestly effective for treatment of dyspareunia. | B | 21 , 32 , 33 |
| Transdermal testosterone, with or without concomitant estrogen therapy, has been shown to be effective for short-term treatment of low sexual desire or arousal in natural and surgically induced menopause. | B | 35 , 36 |

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

Flibaserin (Addyi) for HSDD

- The FDA approved Flibanserin in 2015. Sold under the trade name Addyi, is a medication approved for the treatment of premenopausal women with hypoactive sexual desire disorder (HSDD).
- The medication increases the number of satisfying sexual events per month by about one half over placebo from a starting point of about two to three. The certainty of the estimate is low.
- The side effects of dizziness, sleepiness, and nausea occur about three to four times more often.

Top 10 Things To Know About

Addyi

Addyi is the first FDA approved drug to treat hypoactive sexual desire disorder (HSDD) in premenopausal women. Whether you're considering speaking with your clinician about Addyi or just interested in learning more about this new drug, it is important to know the facts.

Addyi has only been tested in a small subset of women.

The participants who enrolled in the initial clinical trials for Addyi were premenopausal, heterosexual, and generally very healthy women. The overwhelming majority of these women identified as White (>85%), non-Hispanic (>86%), and non-smokers (>85%). Given the extensive list of exclusion criteria for the trials, the extent to which the trials' results can be generalized to the public is unknown.

1



WHITE
NON-SMOKER
HETEROSEXUAL
100%



2

Addyi may cause sudden prolonged unconsciousness.

Addyi causes central nervous system depression. During clinical trials, women who used Addyi were more likely to experience dangerously low blood pressure, dizziness, and even loss of consciousness than women taking placebo. These studies also revealed a higher incidence of accidental injury in women who used Addyi.

Alcohol should be avoided when taking Addyi.

Women may experience fatigue, low blood pressure, and fainting when using Addyi, all conditions which may be exacerbated when drinking alcohol. Women who are moderate drinkers (compared to heavy drinkers) may experience these effects more dramatically. The FDA asked Sprout (the company that owned Addyi) to conduct a safety study assessing these risks, but only two of the 25 participants in the alcohol safety study were women. Because the risks of using alcohol with Addyi are still unknown, the FDA is counting on women to abstain from alcohol permanently despite there being no known strategy to ensure people are able to do this in the long term.

3



Addyi

4

Hormonal contraceptives may interfere with Addyi.

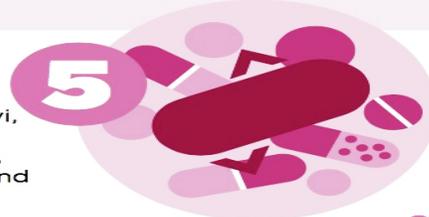
Some adverse events, including sleepiness (somnolence), dizziness and fatigue, were reported more often in women who used hormonal contraceptives. Hormonal contraceptives are known to affect a certain enzyme (CYP3A4) which may increase Addyi exposure by 40%. Young women, many of whom often use hormonal contraceptives, may face additional and unnecessary risk when using this drug.

RISK

Addyi may interfere with a lot of other drugs too.

Many other commonly used medications are also CYP3A4 inhibitors and may significantly increase Addyi exposure. This could lead to poor tolerability of Addyi, as well as increases in low blood pressure and fainting for women using Addyi. These medications include antiepileptic drugs, benzodiazepines, antidepressants, antipsychotics, mood stabilizers, narcotics, vaginal yeast infection medications, and even St. John's wort, all of which were excluded from Addyi's phase 3 studies.

5



over

Cream Treatment for Women

- Prescription vaginal sex enhancing cream called “**Scream Cream**”
- Anecdotal increases in desire and libido, enhance sensitivity, and blood flow.
- **Contains Aminophylline / Ergoloid Mesylate / Larginine / Pentoxifylline / Sildenafil Citrate / Testosterone 30 / 0.5 / 60 / 50 / 10 / 1 mg/mL**
- Dosage: apply **0.25mL – 0.5mL (1-2 clicks)** vaginally 60min prior to sex
- This proprietary formula has been developed by the leading physicians in the field of sexual medicine and interventional endocrinology
- Contains a carefully measured combination of three ingredients which work synergistically to increase direct blood flow and increase sensitivity
- Bio-Identical testosterone can be added to the cream at a customized strength to address any hormone deficiency detected. Libido Cream is compounded at a licensed pharmacy using a HRT base vaginal cream and FDA approved medication



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<http://www.merck.com/mmhe/sec22/ch250/ch250a.html>

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QUESTIONS?



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