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Pharmacologic Therapy in Men's Health:

Hypogonadism, Erectile Dysfunction, and Benign Prostatic Hyperplasia

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INTRODUCTION

Male reproductive, sexual, and urologic health concerns are common presenting complaints in both primary care and subspecialty clinic settings. This article reviews current pharmacologic treatment options for 3 common men's health concerns: hypogonadism, erectile dysfunction (ED), and benign prostatic hyperplasia (BPH).

TESTOSTERONE REPLACEMENT THERAPY IN MALE HYPOGONADISM

Male hypogonadism, defined as signs and symptoms of low testosterone combined with confirmation of low serum testosterone concentration, is estimated to affect 2% to 12.8% of adult men.[1] The prevalence of hypogonadism is higher among certain populations, including the elderly and the obese. It is anticipated that the prevalence of male hypogonadism in the United States will likely increase over the coming years due to a combination of factors, including the aging of the population and increases in comorbid conditions associated with increased risk of hypogonadism such as obesity and diabetes.[1] The evaluation and diagnosis of male hypogonadism are reviewed elsewhere.[2] Here we will focus treatment using testosterone replacement therapy.

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Benefits, Side Effects, and Risks

Among men with symptomatic hypogonadism, the potential clinical benefits of testosterone replacement therapy include increased libido, improved muscle strength, improved body composition (eg, decreased fat mass and increased lean mass), maintenance or improvement in bone mineral density, improved mood and cognition, improved erectile function, and maintenance or improvement in secondary sexual characteristics.[2]

The potential clinical benefits must be carefully weighed against potential risks for each patient. Potential adverse effects of testosterone replacement include erythrocytosis, increases in prostate-specific antigen (PSA), and worsening of prostate disorders (eg, BPH symptoms), worsening of existing obstructive sleep apnea, and dermatologic effects such as acne and skin irritation.[2] Testosterone replacement therapy is not appropriate for hypogonadal men who desire fertility because testosterone suppresses luteinizing hormone production and thus can reduce spermatogenesis by lowering intratesticular testosterone concentration.[3]

In addition, the US Food and Drug Administration (FDA) recently added a warning to all testosterone preparations regarding possible increased risk of cardiovascular disease, including myocardial infarction and stroke in patients taking testosterone. Ongoing studies are attempting to better assess this risk. At this time, clinicians in practice should discuss this warning with all patients when starting or continuing testosterone treatment.[4,5]

Testosterone Preparations

There are a variety of testosterone preparations currently available in the United States (Table 1). The choice of preparation should be determined by the clinician in conversation with each individual patient and should take into consideration patient preference as well as cost and convenience. The most widely used testosterone preparations in the United States are transdermal and injectable preparations due to their ease of use (transdermal) and relatively low cost (injectable).

Injectable preparations—Testosterone enanthate and testosterone cypionate are widely used long-acting injectable testosterone preparations.[6,7] Both forms are administered as intramuscular (IM) injections and most patients are able to administer injections independently at home with the help of a partner. These preparations are highly effective in improving symptoms of hypogonadism and maintaining virilization. In addition, the long-acting preparation allows most men to administer IM injections every 2 weeks (instead of the daily application of a transdermal preparation). With long-acting IM preparations, testosterone concentration and clinical effects (eg, impacts on mood and libido) peak around 1 to 2 days after the injection and wane over the subsequent 2 weeks.[8] For some patients, these fluctuations in testosterone effect are particularly bothersome. In these cases, alternate dosing of 100 mg every week or use of an alternate testosterone preparation may be preferred.

An extra–long-acting IM testosterone preparation, testosterone undecanoate, has also recently been approved for use in the United States. This preparation is administered as a

deep IM injection at baseline, 4 weeks, and then every 10 weeks. This preparation reduces the frequency of IM injection. However, due to risk of pulmonary oil microembolism and anaphylaxis, the drug is only available through a Risk Evaluation and Mitigation Strategy (REMS) program and must be administered by a trained and registered care provider in an office or hospital setting. Thus, this formulation is not recommended unless patients are unable to tolerate or access other available preparations.

Transdermal preparations—There are several transdermal gels currently available in the United States, including Androgel, Testim, Fortesta, and Axiron. Gels are supplied in packets or tubes or in a metered-dose pump and are applied by hand to dry, intact skin on the arms, torso, or thighs. They should not be applied to the scrotum. Gels are generally well-tolerated. They offer the benefit of minimal fluctuation in testosterone concentration from day to day and may be preferable for patients who struggle with peak effects from IM injections. They are occasionally associated with mild skin irritation. Use of gels is limited by the potential for skin-to-skin transfer to others and patients should be instructed to limit this risk by carefully washing their hands after gel application and avoiding skin-to-skin contact with others (particularly female partners or children) on the gel-treated areas.[9] Additionally, some men do not achieve normal testosterone concentrations due to poor absorption of topical applications and monitoring of serum testosterone concentration is important to confirm adequate dosing with these preparations.

One testosterone patch preparation (Androderm) is currently available in the United States. The patch reduces the risk of skin-to-skin transfer of testosterone and is preferable for some patients. However, up to one-third of men who use the patch may have significant rash or skin irritation preventing its ongoing use. Patches should not be applied to the scrotum. Monitoring of testosterone concentration is also important with transdermal patches because absorption can be variable similarly to gel preparations.

Other available preparations—One preparation of subcutaneous testosterone pellet is currently available (Testopel).[10] Pellets are placed in the subcutaneous fat of the buttock, lower abdomen, or thigh every 3 to 6 months. Pellets are placed in sterile conditions in an office or hospital setting. They are associated with risks, including infection, fibrosis, and pellet extrusion. Benefits include avoiding skin-to-skin transfer, no need for self-injection, and infrequent dosing.

Nasal and buccal testosterone preparations are also available. These preparations are infrequently used due to limitations of nasal, sinus, or gingival irritation. In addition, there are limited published data on use of nasal preparation and animal studies suggest possible increases in central nervous system testosterone levels higher than that expected with other preparations.

Oral preparations of testosterone (eg, methyltestosterone) have been available for many years. However, use of these preparations for treatment of male hypogonadism is not recommended because of concerns about possible lack of efficacy in producing virilization, reports of hepatic toxicity with these drugs,[11] and the wide availability of more preferred preparations.

Monitoring and Dose Adjustment

Patients on testosterone replacement therapy should be followed to assess improvement in hypogonadal symptoms and to achieve serum testosterone concentrations in the normal reference range. Among patients being treated with testosterone cypionate or enanthate IM injection every 2 weeks, the clinician should target testosterone levels in the middle to normal range (400–700 ng/dL) 1 week after the last injection.[2] Generally, patients should be seen back approximately 3 months after starting or changing a testosterone dose for clinical assessment; testosterone serum concentration monitoring; if needed; and monitoring of hematocrit and PSA. Once on stable treatment, continued clinical and laboratory follow-up every 6 to 12 months is recommended.[2]

Various formulations of testosterone are available and choice of treatment formulation should be based on discussion of risks and benefits between the provider and each patient. Injectable and transdermal preparations of testosterone are the most widely used in clinical practice and are generally effective and well-tolerated. Alternative testosterone preparations, including subcutaneous testosterone pellets, buccal, and nasal preparations can be considered for patients in whom injectable or transdermal preparations are ineffective or poorly tolerated.

PHARMACOLOGIC TREATMENT OF ERECTILE DYSFUNCTION

Erectile Dysfunction

ED is defined as the inability to achieve and maintain an erection sufficient for intercourse. ED is a common complaint of sexually active men, with a lifetime prevalence of 70%.[12] ED is commonly associated with systemic disorders such as hypertension, diabetes, coronary artery disease, or harmful behaviors such as tobacco or drug use. Other factors that can cause ED include neurologic diseases, hypogonadism, mood disorders, and medications. In addition, the prevalence of ED increases significantly with age, such that most men in their 80s have ED and require treatment if they wish to remain sexually active.[13] Fortunately, there are many efficacious therapies for the treatment of ED in men. Indeed, with current therapies, most men can be successfully treated for ED using 1 of the following therapies.

Approach to Erectile Dysfunction

Before an ED medication is prescribed, it is useful to review the patient’s symptoms, sexual frequency, and erectile function. In particular, low libido may be a sign of underlying hypogonadism, which would trigger a measurement of a morning serum total testosterone concentration and possible treatment with testosterone. In addition, several common medications can adversely affect sexual function, including antihypertensives, antidepressants, antipsychotics, antiandrogens (eg, spironolactone and cimetidine), and opiates. Often, ED can be improved by substitution of 1 of these medications for another that is less likely to interfere with erectile function. For example, selective serotonin reuptake inhibitors commonly impair sexual function, both in terms of ED and anorgasmia. Alternative antidepressants, such as bupropion and venlafaxine are associated with a lower incidence of sexual side effects and may result in improvement in symptoms of ED.[14]

Other important historical clues include prior pelvic surgery or the rapid loss of an erection soon after the initiation of sexual activity, which might suggest either anxiety or a venous leak. On physical examination, evidence of neuropathy or testicular atrophy would suggest systemic disease such as diabetes or hypogonadism. Treating men with low serum testosterone concentrations is likely to improve libido and erectile function, as well as improve muscle and bone density, and is reasonable in patients with truly low serum testosterone. If these approaches to treatment do not result in satisfactory improvement in symptoms, it is reasonable to suggest specific treatment of ED with 1 of the following medications.

Oral Phosphodiesterase Inhibitors

Treatment of ED with as-needed oral phosphodiesterase-5 inhibitors (Table 2) is recommended as initial therapy for ED because these agents are relatively safe, easy to administer, and have a high likelihood of greatly improving symptoms of ED in most men. Phosphodiesterase inhibitors improve erectile function by increasing the production of nitric oxide in the corpora cavernosum, resulting in increased penile blood flow and improved erectile function. The 4 currently available phosphodiesterase-5 inhibitors have some minor differences in terms of their half-life and dosing. In particular, tadalafil has the longest half-life and excellent bioavailability. Therefore, tadalafil can be dosed with food in contrast to sildenafil and vardenafil, which require dosing on an empty stomach 30 to 60 minutes before intercourse.[15] Tadalafil can also be dosed daily at lower doses for men who do not respond to as-needed treatment with some improvement in overall efficacy.[16]

Oral phosphodiesterase inhibitors are contraindicated in men taking nitrates, such as nitroglycerin, because severe hypotension can develop. Similarly, caution should be exercised when combining these medications with alpha-adrenergic antagonists, especially older nonselective alpha-antagonists prescribed for the treatment of prostatic hyperplasia. Because of the potential for hypotension from the combination of alpha-adrenergic antagonists and oral phosphodiesterase inhibitors, it is frequently recommended that the initial dose of a phosphodiesterase inhibitor be reduced by half, then the dose increased slowly from there to the minimum required for an erection sufficient for intercourse. In addition, switching from a nonselective alpha antagonist, to an alpha1 selective antagonist (see later discussion) in men receiving both therapies is recommended.[17] Common side effects of these medications include headaches, dyspepsia, diarrhea, epistaxis, and a blue tinge to vision (with sildenafil). In addition, all of these medications are metabolized by CYP3A4, so coadministration of any of the phosphodiesterase-5 inhibitors with a CYP3A4 inhibitor results in increased drug concentrations, which could increase the risk of side effects such as hypotension.

Other Oral Medications for Erectile Dysfunction

The antidepressant trazadone has been reported to benefit some men with ED and is occasionally prescribed in men with mild depression and ED for a double effect. Side effects of this medication include dizziness, sedation, and weight gain. In addition, priapism has been rarely reported with this medication.[18] Therefore, men should be counseled to seek medical attention for erections that last more than 4 hours while taking this medication.

Finally, yohimbine is occasionally prescribed for ED in the setting of low libido in men with a normal testosterone, although the data supporting this indication are not strong[19] and this medication is not currently approved by the FDA for the treatment of ED. Side effects with yohimbine are frequent and can include potentially serious increases in blood pressure and heart rate. Yohimbine is a common ingredient in nonprescription dietary supplements marketed for sexual potency, so eliciting a history of supplement use in patients with ED may reveal exposure to this drug.

Intraurethral and Intrapenile Alprostadil

Alprostadil (prostaglandin E1) is a direct vasodilator that relaxes vascular smooth muscle to increase blood flow in the penis and results in an erection sufficient for intercourse in most men. Alprostadil is available in both intraurethral forms (tradename Muse in the United States), and intrapenile injection (tradenames Edex and Caverject). Intraurethral alprostadil is introduced into the urethra by an applicator. The penis is then massaged to allow for absorption of the drug into the corpora cavernosum. With treatment, approximately two-thirds of men will experience an erection sufficient for intercourse.[20] Side effects other than penile pain are uncommon. This medication should not be used in men with Peyronie disease, sickle cell anemia, or myeloproliferative disorders due to the risk of priapism.

Intrapenile alprostadil is appropriate for patients who can be trained to perform self-injections and is an especially good choice for those who perform these injections routinely (eg, diabetics using insulin). The sterile alprostadil solution is reconstituted immediately before use and injected into 1 penile corporeal body. Connected circulation between the 2 corpora then delivers the drug to the uninjected side, allowing for a symmetric erection that may last for more than an hour. Almost 90% of men who use intrapenile injections of alprostadil are satisfied with their erectile function with this technique; however, penile pain is a frequent complaint and may lead to discontinuation.[21] Systemic anticoagulation is a contraindication to the use of these injections. Similarly, either form of alprostadil should not be used in men with a penile implant due to the risk of infecting the implant. Intrapenile alprostadil is occasionally combined with other drugs, such as phentolamine and papaverine, by compounding pharmacies; however, these preparations have not been rigorously tested and safety concerns exist regarding these combination therapies, such as penile nodules, hematoma formation (with papaverine), and hepatitis.[22]

Nonpharmacological Therapy for Erectile Dysfunction

Patients who may not respond to pharmacologic therapies, may experience intolerable side effects, may have contraindications to therapy, or may prefer nonmedical therapy do have options for treating ED. Mechanical vacuum pumps can be used to generate an erection sufficient for intercourse, although the necessary occlusive ring placed at the base of the penis often interferes with ejaculation. Penile prostheses are a highly effective form of treated ED. These devices are usually reserved for men who have failed pharmacotherapy and have no contraindications to surgery. Patient satisfaction with these devices is high.

Oral phosphodiesterase inhibitors are initial pharmacotherapy for ED. Intraurethral or intrapenile alprostadil can be used for men who don't have a satisfactory response to oral medications.

PHARMACOLOGIC TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

BPH is a common cause of morbidity in older men. Autopsy studies have shown that the prevalence of BPH starts increasing from 40% to 50% around age 50 to more than 80% older than age 80 years.[23] Using history and digital rectal examinations, the Baltimore Longitudinal Study of Aging also found similar clinical prevalence rates.[24] Symptoms may include a variety of lower urinary tract symptoms, including urinary frequency, urgency, hesitancy, nocturia, and weak urinary stream. The severity of these symptoms can be variable with an insidious onset and slow progression. A meta-analysis of studies that followed untreated men with BPH for 2.6 to 5 years showed that 16% remained stable and 38% showed improvement in symptoms.[25] Therefore, in most men, the decision to treat is based on how much they are affected by their symptoms. The American Urological Association symptoms index, or the International Prostate Symptom Score (IPSS),[26] can be a useful tool to assess the severity of a patient's symptoms and help identify men who may warrant therapy.

Medical Management

In men with mild-to-moderate symptoms (IPSS<19), monotherapy with alpha1-adrenergic antagonists can be the starting point. Men with more severe symptoms may need to start with combination therapy.

Alpha1-Adrenergic Antagonists

Alpha1-adrenergic antagonist drugs relax the smooth muscle in the bladder neck, prostate capsule, and prostatic urethra, countering the dynamic component of bladder outlet obstruction. There are 5 FDA-approved agents in the United States: terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin. When compared with 5-alpha-reductase inhibitors, these agents have a faster onset of therapeutic benefits (6–12 months vs 1–2 weeks) and are more effective at improving urinary symptoms in the short and long term.[27] A meta-analysis of placebo-controlled trials and comparative studies among terazosin, doxazosin, tamsulosin, and alfuzosin showed these agents reduced IPSS scores by 30% to 40% and increased urinary flow rates by 16% to 25%.[28] All the drugs were more effective than placebo and similar in efficacy to each other. Therefore, when choosing between them, cost, side-effect profile, and drug interactions should be determining factors in the decision. Common side effects of these medications include nasal congestion, dizziness, and headache. Table 3 summarizes the different approved agents with their side-effect profiles and costs. The nonuroselective agents, terazosin and doxazosin, need to be initiated at a lower dose and then titrated up over several weeks due to the side effect of hypotension. Taking these medications at bedtime also minimizes the postural lightheadedness that may be seen with initial doses.

5-Alpha-Reductase Inhibitors

5-Alpha-reductase inhibitor medications act by reducing the size of the prostate gland; therefore, therapeutic effects may not be seen until after 6 to 12 months of therapy. This is why these agents are more effective in men with larger prostates. In general, these agents can be used in men who desire medical therapy for BPH but are not able to tolerate alpha1-adrenergic antagonists or for combination therapy in men with severe symptoms (IPSS>20). There are 2 approved agents for use: finasteride and dutasteride. A study of 895 men with BPH treated with finasteride for a year noted increased maximal urinary flow rate, 19% decrease in mean prostate volume, and 23% lowering of obstructive and 18% lowering of nonobstructive symptom scores.[29] A study of more than 3000 men has shown that these benefits are sustained for 4 years[30] and 6 years.[31] Additionally, finasteride therapy may halve the risk of needing prostate surgery and acute urinary retention compared with placebo.[30] Dutasteride seems similar to finasteride on all fronts. A trial comparing finasteride and dutasteride therapy for 12 months showed no differences in reduction of prostate volume, improvement in urinary flow rates, urinary symptoms scores, or adverse-effect profiles.[32] In addition, in patients with gross hematuria secondary to BPH or uncertain cause, finasteride has been shown to reduce the rate of recurrent hematuria as well as the need for surgery.[33]

Side effects of 5-alpha-reductase inhibitors

1. Prostate cancer risk: Two large, randomized controlled trials have shown that in men with BPH, although there is overall lower risk of prostate cancer with 5-alpha-reductase inhibitor therapy, the risk of high-grade prostate cancer (Gleason score>7) is increased.[34,35] This has led to an FDA warning label to ensure men are evaluated for prostate cancer before initiation of therapy. A suggested approach is to perform digital rectal examinations and obtain PSA levels before starting the medication and monitoring these while on treatment. Because these agents can lower PSA by up to 50%, any increase in PSA on therapy warrants further evaluation.
2. Sexual dysfunction: Commonly noted problems include decreased libido, ejaculatory dysfunction, and ED; however, these may only manifest in the first year of therapy.[36]

Anticholinergic Agents

Anticholinergic agents are useful in patients with predominantly irritative urinary symptoms (eg, frequency, urgency, incontinence) either as monotherapy or in combination with alpha1-adrenergic antagonists. Commonly used agents include tolterodine and oxybutynin. Other approved agents are darifenacin, solifenacin, fesoterodine, and trospium. Therapy comes with the side effects of peripheral anticholinergic action, including drowsiness, decreased cognitive function, blurry vision, dry mouth, tachycardia, and constipation.

Phosphodiesterase-5-Inhibitors

Tadalafil is the only approved agent in the phosphodiesterase-5-inhibitor class for use in BPH in the United States. It is worth considering in men with symptomatic BPH and ED. It has been shown to improved urinary flow rate and urinary symptom scores.[37,38]

Herbal Therapies

There is no concrete evidence to support the efficacy of agents such as saw palmetto, beta-sitosterol, cernilton, and pygeum africanum. None of these agents are approved for the treatment of BPH in the United States.

The decision to treat men with BPH is based on severity of symptoms and their impact on a patient's life. Alpha1-adrenergic antagonists are first-line therapy with comparable efficacy of the different agents. Their side-effect profiles and cost may be the determining factors for which agent is chosen for treatment. 5-Alpha-reductase inhibitors are useful in men with large prostates or those unable to tolerate alpha1-adrenergic antagonists.

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KEY POINTS

- Injectable and transdermal preparations of testosterone are the most widely used in clinical practice. Alternative testosterone preparations, including subcutaneous pellets, buccal, and nasal preparations, can be considered for patients in whom injectable or transdermal preparations are ineffective or poorly tolerated.
- Oral phosphodiesterase inhibitors are initial pharmacotherapy for erectile dysfunction. Intraurethral or intrapenile alprostadil can be used for men who do not have a satisfactory response to oral medications.
- Alpha1-adrenergic antagonists are first-line therapy for benign prostatic hyperplasia. 5-Alpha-reductase inhibitors are useful in men with large prostate glands or those unable to tolerate alpha1-adrenergic antagonists.

Table 1

Testosterone preparations

Formulation	Preparation (US Tradename)	Dosage Forms	Usual Dosing[a]	Site of Application	Advantages	Disadvantages and Risks	Approximate Cost per Month[b]
Intramuscular							
Long-acting	Testosterone cypionate (Depo-Testosterone)	100 mg/mL or 200 mg/mL	100–200 mg every 2 wk or 50–100 mg every 1 wk	Thigh or buttock	Home IM injection, infrequent treatment, low cost, high efficacy	Peak effects or fluctuating testosterone levels, pain or irritation at injection site	$15–60 (generic) $50–70 (brand)
	Testosterone enanthate (Delatestryl)	200 mg/mL					$15–35 (generic) $45–50 (brand)
Extra–long-acting	Testosterone undecanoate (Aveed)	250 mg/mL	750 mg initially, then 750 mg at 4 wk, then 750 mg every 10 wk ongoing	Buttock	Long-acting	Administered in office or hospital by REMS-certified provider, risk of pulmonary oil microembolism and anaphylaxis	$1050 (plus cost of injection)
Transdermal							
Gel	Androgel (1% gel)	25 mg in 2.5 g packet OR 50 mg in 5 g packet	50–100 mg daily	Dry intact skin or back, abdomen, upper thighs or arm	Steady serum testosterone concentration	Risk of transfer, requires daily application, may not achieve normal testosterone levels in all men, occasional skin irritation	$175–400 (generic) $500–525 (brand)
	Testim (1% gel)	50 mg in 5 g packet					$160–320 (generic) $480–520 (brand)
	Androgel (1.62% gel)	20.25 mg in 1.25 g packet 40.5 mg in 2.5 g packet 20.25 mg per actuation, metered-dose pump	20.25–81 mg daily				$480–550 (brand only)
	Fortesta (2% gel)	10 mg per actuation, metered-dose pump	10–70 mg daily	Dry intact skin of front and inner thighs	Ease of application,		$160–400
	Axiron (2% solution)	30 mg per actuation, metered-dose pump	30–120 mg daily	Dry, intact skin of axilla	Ease of application reduced risk for transfer		$260–1200
Patch	Androderm	2 mg/24 h patch	2–6 mg daily	Dry intact skin of arm or torso	Limited risk of transfer, no injection	Skin irritation or rash (about 1/3 of men), daily application	$475–510

Formulation	Preparation (US Tradename)	Dosage Forms	Usual Dosing[a]	Site of Application	Advantages	Disadvantages and Risks	Approximate Cost per Month[b]
		4 mg/24 h patch					
Other							
Implanted Subcutaneous Pellet	Testopel	75 mg pellets	150–450 mg every 3–6 mo	Implanted into subcutaneous fat of buttock, lower abdominal wall or thigh	No risk of transfer, no daily treatment	Extrusion, infection, fibrosis at pellet sites Placed in clinic or hospital by trained provider under sterile conditions	$150–175 (plus cost of pellet placement) cost estimate based on dose 150 mg mg every 3 mo
Nasal	Natesto	5.5 mg per actuation, metered-dose pump applicator	11 mg (2 pumps, 1 in each nostril) 3 times daily	Intranasal	Minimal risk of transfer	Frequent administration, rhinorrhea, epistaxis, sinusitis, nasal scab	$600–700
Buccal	Striant SR	30 mg buccal system	30 mg twice daily	Adhere to No injection depression in the gingiva superior to upper incisors		Frequent administration, gingival irritation	$550–600
Oral	Generally not recommended						

Abbreviations: IM, intramuscular; REMS, Risk Evaluation and Mitigation Strategy.

[a] Usual doses are listed but dosing should be adjusted based on specific patient factors and clinician judgment.

[b] Cost data based on average cost purchasing monthly supply, various suppliers as listed on goodrx.com at the time of publication and estimated costs at University of Washington Medical Center for facility administered testosterone undecanoate and Testopel.

Table 2

Medications for the treatment of erectile dysfunction

Drug Name	Tradename	Dose Range	Side Effects	Notes
Oral				
Sildenafil	Viagra	25–100 mg as needed	Headaches, dyspepsia, hypotension, rhinitis, visual disturbance (ie, Viagra)	Avoid coadministration with nitrates & alpha-antagonists
Vardenafil	Levitra	5–20 mg as needed		Use with caution in liver & kidney dysfunction
Tadalafil	Cialis	10–20 mg as needed or 2.5–5 mg daily		Avoid strong CYP3A4 inhibitors
Avanafil	Stendra	50–200 mg as needed		
Trazadone	Desyrel	50–300 mg each night, orally	Sedation, dizziness, weight gain, priapism	Potential for QTc prolongation Less potent than PDE-5 inhibitors
Intraurethral Pellet				
Alprostadil	Muse	125–1000 mcg	Vasodilatation, penile pain, priapism	Can be used twice daily Avoid in hematological disease
Intrapenile Injections				
Alprostadil	Caverject, Edex	5–40 mcg	Injection site pain, priapism	Max use 3 times weekly, and once in 24 h Avoid in anticoagulated patient

Abbreviations: PDE-5, phosphodiesterase type 5; QTc, corrected QT interval.

Table 3

Alpha1-adrenergic antagonists with their side-effect profiles and cost

Drug	Uroselective	Hypotension	PDE-5i Worsen Hypotension	Ejaculatory Dysfunction	Cost per Month
Terazosin	No	↑↑↑	Yes	No	$48
Doxazosin	No	↑↑↑	Yes	No	$118 (ER) $43 (IR, generic) $107 (IR, Cardura)
Tamsulosin	Yes	—	No	Yes	$126 (generic) $226 (Flomax)
Alfuzosin	Yes	↑	No	No	$126 (generic) $690 (Uroxatral)
Silodosin	Yes	—	No	Yes	$227

Abbreviations: ER, extended release; IR, immediate release; PDE-5i, phosphodiesterase-5 inhibitors.

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