

## Oral Medications in the Management of Erectile Dysfunction

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**Editors' Note:** *This month we continue the new feature—STEPPEd Care: An Evidence-Based Approach to Drug Therapy. These articles are designed to provide concise answers to the drug therapy questions that family physicians encounter in their daily practice. The format of the feature will follow the mnemonic STEP: safety (an analysis of adverse effects that patients and providers care about), tolerability (pooled drop-out rates from large clinical trials), effectiveness (how well the drugs work and in what patient population[s]), and price (costs of drug, but also cost-effectiveness of therapy).<sup>1</sup> Hence, the name STEPPEd Care.*

Since the informatics pioneers at McMaster University introduced evidence-based medicine,<sup>2</sup> Slawson and Shaughnessy<sup>3,4</sup> have brought it to mainstream family medicine education and practice. This feature is designed to further the mission of searching for the truth in medical practice. Authors will provide information in a structured format that allows the readers to get to the meat of a therapeutic issue in a way that can help physicians (and patients) make informed decisions. The articles will discourage the use of disease-oriented evidence to make treatment decisions. Examples of disease-oriented evidence include blood pressure lowering, decreases in hemoglobin A<sub>1c</sub>, and so on. We will include studies that provide POEMs—patient-oriented evidence that matters (myocardial infarctions, pain, strokes, mortality, etc)—with the goal of offering patients the most practical, appropriate, and scientifically substantiated therapies. Whenever possible, number needed to treat to observe benefit in a single patient will also be included as a way of defining advantages in terms that are relatively easy to understand.<sup>5,6</sup>

*At times this effort will be frustrating. Even as vast as the*

*biomedical literature is, it does not always support what clinicians do. We will avoid making conclusions that are not supported by POEMs. Nevertheless, POEMs should be incorporated into clinical practice. The rest is up to the reader. Blending POEMs with rational thought, clinical experience, and importantly, patient preferences can be the essence of the art of medicine.*

*We hope you will find these articles useful and easy to read. Your comments and suggestions are welcome. You may contact the editors through the editorial office of JABFP or on the Internet (<http://clinic.isu.edu/drugsteps/intro.html>). We hope the articles provide you with useful information that can be applied in everyday practice, and we look forward to your feedback.*

Rex W. Force, PharmD, STEPPEd Care Feature Editor

John P. Geyman, MD, Editor

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Penile erectile dysfunction, or impotence, is a persistent inability to achieve or maintain an erection sufficient for completion of satisfactory sexual activity. Between 20 and 30 million men experience erectile dysfunction in this country alone,<sup>1</sup> though the diagnosis could be underestimated because

many patients are reluctant to discuss this issue with their physicians. Erectile dysfunction is classified as organic, nonorganic (psychogenic), or mixed. Table 1 lists the various causes of erectile dysfunction; however, it is important to realize most patients with organically caused dysfunction will also have some component of psychogenic dysfunction. Organic causes of erectile dysfunction are found in approximately 70 to 80 percent of patients; in about one third of patients the cause will be purely psychogenic.<sup>2</sup> Although erectile dysfunction is not a fatal condition, an inability to have sat-

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**Table 1. Causes of Erectile Dysfunction.**

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Alcohol abuse
Anxiety or depression
Coronary artery disease
Diabetes
Hormonal abnormalities
Hypertension
Medications: antihypertensives, antidepressants, anti-arrhythmics, antihyperlipidemics, antipsychotics, diuretics, anticonvulsants, antiandrogens, narcotics, NSAIDs, H <sub>2</sub> (histamine) receptor antagonists, recreational drugs
Peripheral vascular disease
Renal or hepatic failure
Sickle cell anemia
Smoking
Surgery (pelvic or perineal)
Trauma to pelvis or spine

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Adapted from Greiner and Weigel.<sup>1</sup>

NSAID - nonsteroidal anti-inflammatory drug.

isfactory sexual relations drastically affects the quality of life of those afflicted and their partners, and considerable emotional and psychiatric morbidity does occur.

In addition to the embarrassment of discussing erectile dysfunction with their physicians, many patients are unwilling to use the more invasive or unspontaneous treatments that have been available. These therapies included penile injections, vacuum constriction devices, and prosthetic implants. Recently, media, advertising, and the arrival of new oral products for the treatment of erectile dysfunction have increased awareness of the disorder and have spurred patients to request treatment. Patients may now choose to start therapy with the least invasive treatment (ie, oral medications) and then progress to more invasive treatments, if necessary. Family physicians are the logical first step in these patients' quest for treatment and might find themselves inundated with requests for the available oral treatments.

Yohimbine (Yocon, Yohimex, and others) is an oral medication for the treatment of erectile dysfunction that has been in use for many years. Other available oral medications include sildenafil (Viagra), which was recently released, and phentolamine (Vasomax). Each agent enhances the ability to produce an erection by increasing blood flow in the penis, albeit through different mechanisms. The mechanism of yohimbine in treating erectile dysfunction appears to be mediated through a central presynaptic  $\alpha_2$ -adrenergic receptor blockade leading to vasodilation within the corpus cavernosum. Sildenafil is an inhibitor of phosphodi-

esterase type 5 (PDE5), which leads to increased levels of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum and results in smooth muscle relaxation and increased inflow of blood. Phentolamine antagonizes  $\alpha_1$ - and  $\alpha_2$ -adrenergic receptors, leading to smooth muscle dilation and increased blood flow. Unlike the injectable and suppository medications, all oral treatments for impotence require sexual stimulation to achieve erection.

## Methods

This review will examine the available oral medications for the treatment of erectile dysfunction - yohimbine, sildenafil, and phentolamine. MEDLINE was searched for articles published from January 1983 through April 1998 using the search terms "yohimbine," "sildenafil," "UK-92,480," "phentolamine," "erectile dysfunction," and "impotence." The search was limited to randomized, double-blind, human clinical trials with these agents used as monotherapy that were published in English language journals. The trials were not limited to the type of erectile dysfunction studied. In addition, studies were selected from various reference lists containing sildenafil and phentolamine. Studies were included if they evaluated patient-oriented evidence that matters (POEMs) as primary outcomes. In erectile dysfunction these outcomes include the number of successful attempts at intercourse, ability to maintain erection to ejaculation, patient satisfaction with treatment, and quality of life. Studies in which patients received active drug only in a clinic setting were excluded. The number of patients needed to treat (NNT) to provide one positive outcome were calculated and presented.

The STEP approach will be used in this review to evaluate the roles of the oral medications in treating erectile dysfunction: safety (an examination of the adverse effects), tolerability (the dropout rates from trials), effectiveness (how well these medications work in patients whose impotence is due to various causes), and price (costs of the drugs and third party reimbursement).

## Safety and Tolerability

When choosing an agent to treat erectile dysfunction, important issues to consider include safety, tolerability, and convenience. Because these medications are used to improve the patient's quality of life, agents that have marked ad-

verse effects, are invasive, or are inconvenient might not be first options. In addition to being noninvasive and convenient, all three oral medications for erectile dysfunction appear to be well tolerated and have minimal and transient side effects at their recommended dosages. Priapism, a concern with the penile injection therapies and urethral suppositories, does not appear to be an issue with the oral medications; therefore, adverse effects might not be a major factor when choosing among these agents.

Many clinical trials evaluating yohimbine did not include information on adverse effects. When examining those trials that did include this information, the most common adverse effects observed with yohimbine included anxiety, increased urinary frequency, tachycardia, and increased arterial pressure.<sup>3,4</sup> In a study by Teloken et al<sup>5</sup> in which patients received 100 mg of yohimbine daily, a dose three to five times higher than used in other trials, 32 percent of patients experienced an increase in urinary frequency compared with 14 percent taking placebo. A fairly high percentage of patients taking yohimbine reported tachycardia (27 percent), whereas none of the patients on placebo experienced an increased heart rate. Only one study of yohimbine included in this review reported patient dropout rates resulting from adverse effects. This study included 82 patients in a crossover design, and 8 patients (10 percent) discontinued therapy because of adverse effects of treatment with yohimbine.<sup>4</sup> The adverse effects were similar to those previously mentioned. In a trial by Rowland et al,<sup>6</sup> the more common adverse effects in the yohimbine group included disturbed sleep, mild diarrhea, lack of energy, and, surprisingly, lower sexual desire.

Sildenafil and phentolamine are generally well tolerated by most patients according to the available clinical trials. Goldstein et al<sup>7</sup> conducted two trials of sildenafil with a total of 861 patients. Adverse effects included headache (12 to 30 percent), flushing (10 to 27 percent), and dyspepsia (3 to 16 percent) with rates being dose dependent. Additionally, dose-dependent transient visual disturbances, or changes in the perception of color hue or brightness, were reported by 2 to 9 percent of men. The manufacturer reports a rate of 3 percent for transient color vision changes. Between 6 and 15 percent of patients withdrew from the trials during treatment with sildenafil compared

with 8 to 17 percent of those receiving placebo. Discontinuation because of treatment-related adverse effects was 1 to 2 percent. Additional reasons for discontinuation included insufficient response, protocol violations, and withdrawal of consent, among others.

Recently there have been several reports of deaths occurring with concurrent sildenafil and nitrate use. These drugs in combination cause potentially fatal decreases in blood pressure. According to the manufacturer, sodium nitroprusside use is also contraindicated, but other nonnitrate vasodilators ( $\beta$ -blockers,  $\alpha$ -blockers, angiotensin-converting enzyme inhibitors, diuretics, and calcium channel blockers) have not been shown to be a problem. Sildenafil should never be administered to a patient concurrently taking nitrates or sodium nitroprusside or to a patient who might inadvertently receive a nitrate after exertion or sexual activity.

Nasal congestion was reported as the only adverse effect, with one patient experiencing it, in the smallest study of phentolamine.<sup>8</sup> In two trials reported by Zorogniotti,<sup>9</sup> 6 percent of patients complained of nasal congestion and 2.3 percent complained of faintness or dizziness, relieved by lying down. Another study excluded patients with intolerance to phentolamine (increased blood pressure and pulse) before randomization by giving a test dose; therefore, no adverse effects were mentioned in the results.<sup>10</sup> This methodology could limit the generalizability of these results to general practice. Information available from the manufacturer of phentolamine lists insomnia, nasal congestion, and dyspepsia as common adverse effects.

### Effectiveness

Primary efficacy outcomes in trials involving erectile dysfunction medications vary dramatically from one trial to another. Many include measures of penile rigidity using plethysmography, whereas others evaluate patient-oriented outcomes. Patient-oriented outcomes range from patient-perceived improvement in rigidity of erection, to their perceived improvement in sexual function, to the actual number of successful attempts at vaginal intercourse during a given period. All studies evaluate efficacy differently. In addition, the medications have not been compared head-to-head, so data on comparative efficacy are unavailable.

**Table 2. Summary of Trials Examining Effects of Yohimbine on Erectile Dysfunction.**

Study	Study Duration (wk), Design	No. of Patients, Cause	Study Group	Outcome	Yohimbine %	Placebo %	NNT
Mann et al <sup>3</sup>	8	30, organic, nonorganic	Placebo, yohimbine 5 mg tid	Improvement in CGI			
				All patients	60	40	NS
				Nonorganic	86	33	2
				Organic	38	44	NS
Morales et al <sup>11</sup>	10 Partial crossover	100, organic	Placebo, yohimbine 6 mg tid	Positive response			
				Complete	20	14	NS
				Partial	23	14	NS
Reid et al <sup>12</sup>	10	48, nonorganic	Placebo, yohimbine 6 mg tid	Complete or partial improvement in sexual functioning			
				Phase I	62	16	2
				Overall	46	16	NS
Susset et al <sup>4</sup>	4 Partial crossover	82, organic, nonorganic	Placebo, yohimbine 5.4 mg qid increased to 10.8 mg qid	Full or partial response	34	NR	NA
Teloken et al <sup>5</sup>	4 Crossover	22, organic	Placebo, yohimbine 100 mg daily	Complete response	14	5	NS
				Partial response	55	41	NS
				No response	18	50	NS
				Worse	14	0	NS

CGI - Clinical Global Impression improvement scale, NA - not available, NNT - number needed to treat, NR - not reported, NS - not significant.

### Yohimbine

Yohimbine is the oldest oral medication for erectile dysfunction and has shown conflicting results with regard to efficacy since its first use decades ago. Table 2 summarizes the results of the trials that evaluate the effectiveness of yohimbine in treating erectile dysfunction using patient-oriented outcomes. Each trial used a different primary outcome to assess efficacy, studied different populations, and used varying doses and schedules of yohimbine. Studies that did not report percentage of improvement were not included in Table 2 since NNT values could not be calculated.<sup>6</sup>

To help qualify which patients might benefit most from yohimbine treatment, a closer examination of the trial by Susset et al<sup>4</sup> is beneficial. In this study of 82 patients with erectile dysfunction of mixed causes, patients received either placebo or 5.4 mg of yohimbine four times daily. The dose of yohimbine was gradually increased to 10.8 mg four times daily throughout the 4-week study. Positive results were found in 34 percent of patients taking yohimbine. The authors, who also examined the effects of various factors on their results, found that patients who had mild dysfunction, short duration of erectile dysfunction (less than 2 years), lower levels of arterial insufficiency, and high-normal testosterone levels re-

sponded significantly better.

From this evidence it is apparent that yohimbine was not a very effective agent for patients who had organic erectile dysfunction, even with doses increased to 100 mg daily. In contrast, those patients who had psychogenic or nonorganic dysfunction seemed to experience some increase in function with yohimbine. Only one of the trials including psychogenic dysfunction did not show a statistically significant improvement when patients attempted intercourse, but it did show some improvement when patients masturbated.

### Sildenafil

Four published trials are available for evaluating sildenafil (Table 3). The first, a four-way crossover trial of 12 patients, did not measure patient-oriented outcomes. Instead, it focused on in vitro studies relating to the mode of action of sildenafil, pharmacokinetic studies in human volunteers, and a clinical study in patients with erectile dysfunction.<sup>13</sup> Using plethysmography, the mean duration of rigidity of greater than 60 percent at the base of the penis was significantly longer in the patients taking sildenafil.

The first trial that included patient-oriented outcomes studied 12 patients with no established organic cause of erectile dysfunction.<sup>14</sup> Patients

**Table 3. Summary of Trials Examining the Effectiveness of Sildenafil and Phentolamine on Erectile Dysfunction.**

Study	Duration, Design	Number of Patients, Cause	Study Group	Outcome	Placebo %	Medication %	NNT
<i>Sildenafil</i>							
Boolell et al <sup>14</sup>	1 wk, crossover	12 patients, nonorganic	Placebo, sildenafil 25 mg/d	Improvement in erections	17	83	1.5
Goldstein et al <sup>7</sup>	24 wk	532 patients, organic, nonorganic, mixed	Placebo, sildenafil (25 mg, 50 mg, 100 mg)	Erection sufficient for intercourse	50	72 (25 mg) 80 (50 mg) 85 (100 mg)	4.5 3 3
				Improved erections	25	56 (25 mg) 77 (50 mg) 84 (100 mg)	3 2 2
	12 wk	329 patients, organic, nonorganic, mixed	Placebo, sildenafil 50 mg, then titrated	Successful attempts	22	69	2
				Improvement in erections	19	74	2
<i>Phentolamine</i>							
Becker et al <sup>10</sup>	3 doses	40 patients, idiopathic dysfunction	Placebo, phentolamine (20 mg, 40 mg, or 60 mg)	Success per total attempts	13	20 (20 mg) 30 (40 mg) 37 (60 mg)	NS NS
Gwinup <sup>8</sup>	Single dose, crossover	16 patients, nonorganic	Placebo, phentolamine 50 mg	Erection sufficient for intercourse and maintained until ejaculation	19	69	2
Zorgniotti <sup>9</sup>	Single dose, crossover	85 patients, organic, nonorganic	Phentolamine 50 mg, phenoxybenzamine 10 mg	Full erections sufficient for intercourse		42 9	3
		68 patients, organic, nonorganic	Phentolamine 20 mg (buccal), placebo (buccal)		13	32	

NNT - number needed to treat, NS - not significant.

were excluded if they had diabetes, hypertension, or alcohol abuse. The first phase of the trial was an in-hospital phase in which penile rigidity was measured using plethysmography after varying doses of sildenafil. The second phase consisted of a two-way crossover in which patients received single daily doses of sildenafil 25 mg or placebo at home for 7 days. Patients took the dose 1 to 2 hours before anticipated sexual activity each day and kept a diary of their activity and graded their erections. Improved erectile activity was reported by 10 of 12 (83 percent) patients receiving sildenafil compared with 2 of 12 (17 percent) receiving placebo ( $P = 0.018$ ) resulting in an NNT of 1.5. The mean number of erections graded adequate during the 7-day treatment period was significantly higher at 1.6 in the sildenafil group compared with 0.3 in the placebo group.

Goldstein et al<sup>7</sup> conducted two trials on pa-

tients with organic, psychogenic, and mixed erectile dysfunction. The first trial was a 24-week dose-response study that included 532 men taking either 25-, 50-, or 100-mg doses of sildenafil or placebo as needed (generally 1 to 2 hours before anticipated sexual activity). All doses of sildenafil resulted in significantly greater changes from baseline than did placebo in regard to frequency of penetration and maintenance of erection after penetration ( $P < 0.001$ ). The proportion of men achieving erections hard enough for sexual intercourse during the last 4 weeks of treatment was also significantly higher in the sildenafil groups, at 72 percent, 80 percent, and 85 percent for doses of 25 mg, 50 mg, and 100 mg, respectively, compared with 50 percent for placebo ( $P < 0.001$ , NNT = 4.5, 3.0, and 3.0 for each dose, respectively). Improved erections were reported by 56 percent, 77 percent, and 84 percent of patients,

respectively, compared with 25 percent receiving placebo ( $P < 0.001$  for treatment effect).

The second trial conducted by Goldstein et al<sup>7</sup> lasted 12 weeks and included 329 men. They were given placebo or 50 mg of sildenafil, escalated to 100 mg depending on tolerance and efficacy, to be taken on an as-needed basis. Men receiving sildenafil had significantly greater improvements from baseline with respect to frequency of penetration and maintenance of erections after penetration ( $P < 0.001$ ). When stratified according to cause of erectile dysfunction, patients with mixed erectile dysfunction (organic plus psychogenic) were the only ones who did not have a higher frequency of penetration when taking sildenafil. During the last 4 weeks of treatment, 22 percent of all attempts at intercourse of patients receiving placebo were successful compared with 69 percent of those receiving sildenafil ( $P < 0.001$ ), which resulted in an NNT of 2. In addition, 74 percent of patients receiving sildenafil reported improvement in erections compared with 19 percent of those receiving placebo ( $P < 0.001$ , NNT = 2).

Sildenafil is an effective treatment of erectile dysfunction of various causes despite placebo response rates of up to 50 percent. From the available studies it is apparent that the treatment effect is dose dependent with a greater effect with doses of 50 to 100 mg. Two patients would need to be treated with sildenafil to show improvement of erections in 1 patient, and 3 would have to be treated to provide erections sufficient for intercourse. As is found with most of the treatment options for erectile dysfunction, patients with nonorganic dysfunction responded the best.

### **Phentolamine**

Phentolamine is the newest of the oral treatments for erectile dysfunction. Four published trials are available for evaluating its effectiveness (Table 3). A study of 40 patients was conducted in which patients received three doses each of 20-, 40-, or 60-mg phentolamine fast-dissolving tablets or placebo.<sup>10</sup> Exclusion criteria included erectile dysfunction for longer than 3 years, extensive cardiovascular disease, diabetes or neurologic diseases, obvious psychogenic impotence, or intolerance to phentolamine. Patients started with an initial single-blinded placebo phase in which they were given a placebo tablet; if they achieved one or more successful attempts at intercourse, regard-

less of amount of difficulty in penetration, they were excluded from the study. Patients were also given an initial test dose of phentolamine, and if they were intolerant of the medication (increased blood pressure or pulse), they were also excluded. Clearly these exclusions limit the generalizability of these data.

According to diaries completed by patients at home, success rates per total number of attempts at intercourse were 13 percent, 20 percent, 30 percent, and 37 percent in patients receiving placebo or 20 mg, 40 mg, or 60 mg of phentolamine, respectively. The low number of patients in the study did not allow a statistical analysis, but a trend toward improved function with the use of phentolamine was found. Results might have been more generalizable to patients seen in clinical practice had the investigators included patients responding to placebo initially. Many patients complaining of erectile dysfunction will not be completely impotent but might not achieve full erections or maintain their erection. Also, by using success rates per total number of attempts, additional weight could have been given to those patients who responded well and who had fewer attempts at intercourse.

Another very small study has been conducted to evaluate the effectiveness of oral phentolamine in patients with nonspecific erectile dysfunction.<sup>8</sup> Only patients with erectile dysfunction for longer than 3 months who could not achieve an erection firm enough to penetrate a female partner and maintain that erection until ejaculation were included. None had serious medical problems. Sixteen patients received a 50-mg dose of phentolamine and a placebo dose (betacarotene) 3 to 5 days apart with attempts at intercourse after each tablet. Successful treatment was defined as the ability to achieve, with any form of sexual stimulation, an erection that would allow penetration of a female partner and that could be maintained until intravaginal ejaculation occurred. Sixty-nine percent of patients taking phentolamine and 19 percent of patients taking placebo were successful ( $P = 0.004$ ), resulting in an NNT of 2.

Zorgniotti<sup>9</sup> conducted two trials on patients with varying causes of erectile dysfunction, including those with diabetes or vascular or nonspecific causes. The first trial was an open-label trial comparing phentolamine hydrochloride 50 mg with phenoxybenzamine 10 mg orally. Eighty-five patients were asked to take each drug at least 3 days

**Table 4. Cost of Impotence Agents**

Drug	Dose	Cost
Sildenafil (Viagra)	50 mg	\$8.50-\$15 per tablet
Yohimbine (Yocon, Yohimex, others)	16.2 mg/d*	\$15/mo†
Phentolamine (Vasomax)	40-80 mg	Not available

\*Yohimbine 5.4 mg, three times daily.

†Dosed daily.

apart and 1.5 hours before attempting coitus. Forty-two percent of patients were able to achieve full erection sufficient for intercourse with phentolamine compared with 9 percent taking phenoxybenzamine, resulting in an NNT of 3. The second trial was single blinded and included different patients from the first trial but with the same causes of erectile dysfunction. Buccal phentolamine mesylate 20 mg was compared with placebo. Patients were asked to place the tablet between their gum and cheek 20 to 30 minutes before coitus, each on a different day. Full erections were achieved by 32 percent and 13 percent of patients when receiving phentolamine and placebo, respectively, yielding an NNT of 5.

The response rate seen with the use of phentolamine for erectile dysfunction was not as great as that seen with sildenafil, but in the small number of patients that have been studied, the response was significant. Once again, patients with nonorganic dysfunction received the greatest effect, with that effect possibly being dose dependent as well. Two to 5 patients would need to be treated with a single dose of phentolamine to achieve an erection sufficient for intercourse in 1 patient. The oral route provided a much better response than was observed with the use of buccal phentolamine of lower dosages.

### Price

The costs of the oral agents for impotence are listed in Table 5. Because phentolamine is not yet on the market, a definitive price is not available for this agent. Phentolamine and sildenafil are dosed as needed up to a maximum of one dose daily. Theoretically the patient taking sildenafil will pay up to \$450 a month if the medication is used daily. Conversely, yohimbine is given in a scheduled dosing regimen and costs about \$15 a month, making it the least expensive agent of the three.

Many third party payers will reimburse for yohimbine as a treatment of erectile dysfunction, but most are not reimbursing for sildenafil at this time. Those few companies that have agreed to pay for sildenafil require a letter of medical necessity and might limit monthly quantities. While the high cost of sildenafil and lack of insurance reimbursement make patients somewhat more concerned about the cost of their treatment, many are willing to pay substantial amounts to regain a normal sexual function.

### Summary

According to available published literature, yohimbine is 60 to 80 percent effective in psychogenic erectile dysfunction and not effective in erectile dysfunction of organic causes. Sildenafil is 56 to 85 percent effective in studies of combined populations, and greater than 80 percent effective in patients with purely nonorganic dysfunction. Phentolamine is 30 to 40 percent effective in combined populations and 70 percent effective in purely nonorganic dysfunction. A STEPS overview is provided in Table 5. The placebo response in these trials ranges from 13 to 50 percent. Caution should be used when interpreting or comparing these results, as the agents have not been compared head-to-head in any trial, and with the exception of the

**Table 5. Drug STEPS Overview**

<b>Safety and Tolerability</b>	Yohimbine - can cause anxiety, urinary frequency, tachycardia, increased arterial pressure Sildenafil - can cause headache, dyspepsia, flushing, rarely color vision changes Phentolamine - can cause nasal congestion, dyspepsia, insomnia
<b>Effectiveness</b>	Yohimbine - limited efficacy in psychogenic dysfunction only, NNT = 2 Sildenafil - effective in organic and nonorganic dysfunction, NNT = 1.5-3 when dosed 50-100 mg Phentolamine - effective in organic and nonorganic dysfunction, NNT = 2-5
<b>Price</b>	Yohimbine - \$15/mo (dosed daily) Sildenafil - \$12 per tablet (dosed as needed) Phentolamine - not available
<b>Summary</b>	Sildenafil is well-tolerated, and is the most effective oral agent available with an 80% to 85% response rate in patients with organic or nonorganic dysfunction, resulting in an NNT of 1.5-3 to improve erections, increase number of erections sufficient for intercourse, and increase the number of successful attempts

NNT - number needed to treat.

sildenafil trials, they have been fairly small. Additionally, effectiveness in many trials was judged simply by an improvement in function, not as a return to full sexual function. Even with responders, the improvement rates were not equivalent to sexual functioning in men with no documented erectile dysfunction.

Vacuum constriction devices have a success rate of greater than 80 percent for achieving an erection sufficient for intercourse, and penile injection therapy has been shown to have success rates of up to 89 percent for all causes of dysfunction.<sup>1</sup> Compared with these therapies, the oral medications do not look as promising. Despite the possible inferiority of these medications compared with the other available options, however, many patients will choose oral medications before moving on to the more invasive or less spontaneous options. As a result of the recent release of sildenafil and subsequent explosion in its prescribing, the demand for other noninvasive therapies might increase. Many patients are unsatisfied with the more invasive therapies, and dropout rates for injection therapy have been found to be as high as 80 percent.<sup>15</sup> Family physicians are often the first health care provider approached about erectile dysfunction; they now have a safe and fairly easily monitored treatment option to offer their patients. Although sildenafil is fairly expensive, all three oral treatments for erectile dysfunction are well tolerated with only mild and transient adverse effects when dosed as recommended.

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