

ED:

Remedies for Relief

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The recent addition of two new phosphodiesterase type 5 (PDE-5) inhibitors to the market has offered more choices to men suffering from erectile dysfunction (ED). Practitioners and patients wonder how the three available medications are different, how they should be prescribed and what patient should get which medication.

What medications are best for treating ED?

The answer to his question is not straightforward. In terms of efficacy, all three molecules are likely equally effective in treating men with ED. All have evidence in men with ED from a variety of etiologies, so there is no particular medication based on the cause of ED. In other words, there is no therapy that is uniquely more effective in vasculogenic or neurogenic ED. Furthermore, there have not been any well-constructed, blinded trials that directly compare the efficacy of each of the PDE-5 inhibitors against one another in the same population. However, this doesn't mean that the three molecules are interchangeable.

The medications are best differentiated according to their pharmacokinetic properties (Table 1). The two medications with the shorter half-life (sildenafil and vardenafil) may appeal to men who don't want a medication in their system for a long time. Men who are interested in medication that allows multiple attempts over a window of 36 hours or would like some flexibility in having intercourse some time after taking a pill may prefer the PDE-5 with a longer half-life (tadalafil).

If couples would like the flexibility of taking a

John's Problem

John, 58, is in a stable relationship. He has an eight-year history of Type 2 diabetes mellitus, with early renal complications. He reports a decrease in tumescency and an inability to maintain his erection until orgasm. This has developed slowly over the last few years to the point where it has become increasingly frustrating for John and his wife. With all the ads on TV about erectile dysfunction (ED) therapy, he feels that he should approach you about this problem.



After direct questioning, you learn that his desire is normal and unchanged. He is unable to obtain a good erection with self-stimulation and he does not awaken with erections like he used to, five years ago. John's wife is supportive of John getting treatment and he has no contraindications to ED therapy.

After reviewing the history, you decide that John would be a candidate for oral ED therapy. You advise him that there are three medications available. He asks, "Which one is best, doc?"

For more on John, go to page 95.

medication that is unaffected by meals, consideration should be given to how food affects the absorption of each of the molecules. The onset of action of sildenafil is most affected by particularly fatty meals. Vardenafil is only affected by high-fat meals, while tadalafil is unaffected by meals.

Much has been said about couples' desires for a medication that allows spontaneity. However, the properties of each of the PDE-5s do not intuitively

ED Note...

Remember that anxiety is erectolytic. The more noradrenalin coursing through your patient, the less likely they are to get an erection. This is the explanation for performance anxiety. By identifying and normalizing a patient's emotional response to ED, the overall anxiety and fear around the treatment response can be reduced and the efficacy of the therapy improved.

Table 1
PDE-5 Inhibitors

Property	Sildenafil	Tadalafil	Vardenafil
T 1/2	4 hours	17.5 hours	4 hours
T max (Median rounded numbers)	1 hour	2 hours	1 hour
Onset	30-60 minutes	30 minutes	20-60 minutes
Duration	6 hours	36 hours	5 hours
Absorption	Fatty meals will delay onset of action	Not affected by food	No effect unless a high-fat meal
Usual start dose (If not on a CYP 3A4 inhibitor)	50 mg	20 mg	10 mg
Maximum frequency of dosing	Daily	Daily (special populations excepted)	Daily
Available doses	25 mg, 50 mg, 100 mg	10 mg, 20 mg	5 mg, 10 mg, 20 mg
Maximum dose	100 mg	20 mg	20 mg
Side-effects	<ul style="list-style-type: none"> • Headache • Flushing • Dyspepsia • Rhinitis • Respiratory tract infection 	<ul style="list-style-type: none"> • Headache • Dyspepsia • Back pain • Myalgia • Nasal congestion • Flushing 	<ul style="list-style-type: none"> • Headache • Flushing • Dyspepsia • Rhinitis • Nausea
Use with alpha blockers	With caution with non-selective	With caution with non-selective	Not recommended with all alpha blockers

PDE-5: Phosphodiesterase type 5
T: Testosterone

answer this call. While each of the medications has a different time of maximum concentration, all have data showing their onset to be rapid (less than 15 minutes after ingestion of the pill) in some patients.

Even if a difference did exist, does one, two or ten minutes make a difference to most couples? Does the food interaction make a difference to every couple, every time? Is a long half-life a benefit in allowing a greater window for attempts or is it a disadvantage to have a drug in your system for a longer period of time?

What if treatment fails?

Incomplete response or outright treatment failure does occur with PDE-5 therapy. Failure of therapy is often accompanied by significant emotional distress. For many men, it takes great courage to bring up the subject of ED in the first place. The feelings of loss and hopelessness that many men feel with ED are often amplified when the initial therapeutic trial does not solve the problem. Fortunately, most cases of apparent treatment failure can be remediated.

What causes treatment failure?

One common cause of apparent treatment failure is an inadequate trial of therapy—the more trials, the more successes. I will encourage patients who are initiated on PDE-5 therapy to try the medication four times prior to assessing therapy. Samples are useful, since men are often reluctant or resistant to approach their local pharmacist with a prescription and then pay a substantial amount of money for a medication with unproven efficacy. Sampling overcomes this barrier.

Other causes of apparent treatment failure are listed in Table 2.

What other treatments can be used?

It should be remembered that for patients who are truly unresponsive to oral therapy, other treatments are available, effective and, often, well-tolerated. These include injection therapy and surgical prosthesis. Counselling

More on John

After briefly explaining the difference between the three PDE-5 inhibitors and providing written patient instructions, a prescription and followup appointment, John returns as scheduled. He reports that while not experiencing any side-effects from the medication prescribed, he did not find that it worked. Discouraged, he wonders if he should try one of the other pills or “just forget about the whole thing.”

To find out what happened to John, go to page 96.

Table 2

Reasons for apparent treatment failure with oral therapy

- Inadequate dose
- Inadequate arousal or stimulation
- Inadequate timing between the dose and attempted intercourse
- Not enough trials (more trials equal more success)
- Androgen deficiency
- True treatment resistance—severe vascular, endothelial or neurologic disease
- Reliability (sometimes the drug won't work on a given attempt, but will work generally)
- Erectolytic factors outweigh the effect of oral therapy (stress, fatigue, alcohol)
- Wrong diagnosis (premature ejaculation, desire disorder)
- Side-effects outweigh the benefits of treatment

ED Note...

In some cases where there is a strong anxiety component, I will encourage men to use a PDE-5 and self-stimulate without their partner present or without the expectation of penetrative intercourse. I educate patients that taking the performance anxiety away from the first PDE-5 experience will help men gain confidence that the therapy will be effective.

may play a role for some couples where inadequate response to oral therapy results in ongoing emotional distress.

To conclude...

Erectile dysfunction is a common condition. New therapies have given men who suffer from ED more options for treatment. The new PDE-5 therapies offer more choice and flexibility for couples, although efficacy is similar with all the medications in this class. It is important to be both sensitive to incomplete response to therapy and also to pursue causes for apparent treatment failure.

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ED Note...

Men will often have a preference based on their values or what they have heard or read. Reinforcing that all three medications are safe and effective and scheduling a followup after initiation of therapy, improves the likelihood of treatment success.

What Happened to John?

It was determined that John only tried the medication twice. The second time he had a partial response. At that visit he was encouraged to try the same medication for another trial. If that attempt did not result in a good erection, John was encouraged to increase the dose and try again.

In six weeks, John returned to report good success from the increased dose of the originally prescribed therapy with no side-effects.