



Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: Phosphodiesterase 5 Inhibitors
-August 2014-



Background:

In August 2014, the IHS National Pharmacy and Therapeutics Committee reviewed the four currently available phosphodiesterase 5 inhibitors (PDE5Is) and their role in treatment of erectile dysfunction (ED) after receiving a request for evaluation of this topic. The PDE5Is with FDA approval for ED include avanafil (Staxyn®), sildenafil (Viagra®), tadalafil (Cialis®), and vardenafil (Levitra® and Stendra®).

Discussion:

ED is a problem that affects many men and increases in incidence with each decade of life. From the National Health and Nutrition Survey (NHANES) in 2001-2002, it was estimated that about 18% of men 18 years of age and older are affected. Previous reports estimate anywhere from 8-53% of men have ED. About half of men with diabetes have experienced ED. Within all the age groups reviewed, men with ED had a higher prevalence of cardiovascular risk factors. At least 1 cardiovascular risk factor was reported in 90% of the men included in the survey. One very strong independent risk factor for ED is lack of physical activity. The estimated cost of ED in the United States would be \$15 million if all men sought treatment.

ED can have organic or psychogenic causes or both. There are multiple diseases and lifestyle choices that can be implicated in causing ED. This includes diseases such as diabetes, hypertension, nerve disease, multiple sclerosis, atherosclerosis, heart disease, and hormonal abnormalities. Increasing age, injury and psychological factors such as stress, anxiety, guilt, and low self-esteem are also implicated. Potentially modifiable causes include smoking, excessive alcohol intake, obesity, lack of exercise, and side effect of medications.

PDE5Is have been studied for ED in many different disease states. These include diabetes mellitus, chronic kidney disease, post-cancer, multiple sclerosis, and spinal cord injuries. They have also been reviewed for treating ED caused by antidepressants. In all of these, PDE5Is have been found to have some benefit in the treatment of erectile dysfunction.

Guidelines:

Both the European Association of Urology (EAU) and the American Urological Association (AUA) have published guidelines for managing ED. The EAU cites ED as a symptom, not a disease, and stresses finding the underlying cause. Each guideline stresses the importance of fully evaluating the patient prior to initiation of treatment. Once it is decided to treat for ED, both guidelines recommend PDE5Is as first line medical management, unless there are contraindications to use.

There are several other treatment options for ED. Alprostadil, in the form of either intra-urethral suppositories or intercavernous injections, is another drug with evidence to support use in the treatment of ED. Testosterone is another agent with some benefit in treating ED, though it has been found more effective for those with hypogonadism when used in conjunction with a PDE5I. Therapies that are not recommended to treat ED include yohimbine and herbal therapies such as Korean red ginseng.

Nonpharmacologic treatments include vacuum constriction devices, penile prosthesis, venous ligation and penile revascularization (rarely indicated), psychotherapy, and lifestyle changes. Psychotherapy in addition to PDE5I therapy has shown better results than PDE5I alone. Lifestyle modifications include physical activity, control of diabetes, and prevention of cardiovascular disease.

PDE5Is should not be given to patients taking nitrates. They should be used with caution in patients taking alpha-blockers. All PDE5Is have interactions with CYP3A4 inhibitors. They are

contraindicated with some inhibitors and may require dosing changes with others. If a PDE5I is prescribed, medication reconciliation is extremely important in order to provide appropriate dosing. Renal and hepatic function must also be considered as dosage adjustments are required for many of the PDE5Is. Any patient who has angina during intercourse or has had any arrhythmias in the prior 6 months should not be prescribed a PDE5I. Caution should be used in patients with preexisting cardiovascular disease. Avanafil is not recommended for use in patients with NYHA Class 2 or greater heart failure.

The PDE5Is all have similar reports of adverse drug reactions. The most common include flushing, headache, rhinitis, dizziness, back pain, and myalgia. Serious reactions, which patients should be educated on prior to initiation of therapy, include non-arteritic ischemic optic neuropathy (NAION), hearing loss, and priapism. NAION can result in changes or loss of vision. It is unknown if it is related directly to PDE5I use, underlying vascular risk factors, or anatomical defects. Patients should be advised to stop the PDE5I and see immediate medical care if they experience any visual changes or loss. Sudden decrease of loss of hearing was reported in temporal association with PDE5I use. Again, advise patients to seek medical care if any hearing loss occurs. Patients should seek care for any erection that lasts for longer than 4 hours.

Findings:

The NPTC had a lengthy discussion about the use of PDE5Is and elected not to add any PDE5Is to the National Core Formulary at this time. The committee does hope that providers recognize the psychological effects ED may have on their patients. The committee recommends educating patients on potential causes of ED and encouraging patients to modify those factors over which they may have some control.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

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