Stendra (avanafil)

STRENGTH	DOSAGE FORM	ROUTE	GPID
50 mg, 100 mg, 200 mg	tablets	oral	35716, 35719, 35725

MANUFACTURER

Vivus, Inc.; Auxilium Pharmaceuticals, Inc.

INDICATION

Stendra (avanafil) is a phosphodiesterase-5 (PDE-5) inhibitor indicated for the treatment of erectile dysfunction

DRUG CLASS

Endocrine Disorder- Fertility; Drugs to Treat Impotency

PLACE IN THERAPY

Stendra is the fifth PDE-5 inhibitor to be approved for erectile dysfunction (ED). Stendra joins Viagra (sildenafil - approved March 1998), Cialis (tadalafil-approved November 2003), Levitra (vardenafil-approved August 2003) and Staxyn (vardenafil oral disintegrating tablet- approved June 2010). In the treatment of ED, there is currently no generic agent available. Stendra was approved in April of 2012 and has recently been introduced to the market. Like Viagra, the FDA label recommends taking the drug 30 minutes prior to sexual activity. However, Stendra was able to produce an erection 20-40 minutes after dosage and successful intercourse was observed as early as 15 minutes after administration.

According to the FDA, it is estimated that 30 million men in the United States are affected by ED. Erectile dysfunction, one of the most common sexual disturbances in the adult male, is defined as a man's consistent or recurrent inability to attain and/or maintain penile erection sufficient for satisfactory sexual performance. Epidemiologic studies have shown the overall prevalence of ED is approximately 20–40% at 40 years of age and 70% at 70 years. With the elderly population continuously growing it is estimated that by 2025 an estimated number of 320 million men will be affected by ED.

EFFICACY

The approval of Stendra was based on 3 randomized, double-blind, placebo-controlled, parallel group trials of up to 3 months in duration. Stendra was taken as needed at doses of 50 mg, 100 mg, and 200 mg. Patients were instructed to take 1 dose of study drug approximately 30 minutes prior to initiation of sexual activity. Food and alcohol intake was not restricted.

The 3 primary outcome measures were the erectile function domain of the International Index of Erectile Function (IIEF) and Questions 2 and 3 from Sexual Encounter Profile (SEP). The IIEF erectile function domain has a 30-point total score, where the higher scores reflect better erectile function. The SEP included diary-based measures of erectile function. Question 2 of the SEP asks "Were you able to insert your penis into your partner's vagina?" Question 3 of the SEP asks "Did your erection last long enough for you to have successful intercourse?"

Results in the General ED Population:

Stendra was evaluated in 646 men with ED of various etiologies (organic, psychogenic, mixed). The mean age was 55.7 years (range 23 to 88 years). The population was 85.6% White, 13.2% Black, 0.9% Asian, and 0.3% of other races. The mean duration of ED was approximately 6.5 years. Stendra at doses of 50 mg, 100 mg, and 200 mg demonstrated statistically significant improvement in all 3 primary efficacy variables relative to placebo .

Mean Change From Baseline for Primary Efficacy Variables in General ED Population (from Stendra prescribing information)

	Placebo (N=155)	STENDRA 50 mg (N=154)	STENDRA 100 mg (N=157)	STENDRA 200 mg (N=156)
IIEF EF Domain Score				
Endpoint	15.3	18.1	20.9	22.2
Change from baseline†	2.9	5.4	8.3	9.5
p-value*		0.0014	<0.0001	<0.0001
Vaginal Penetration (SEP2)				
Endpoint	53.8%	64.3%	73.9%	77.3%
Change from baseline†	7.1%	18.2%	27.2%	29.8%
p-value*	-	0.0009	<0.0001	<0.0001
Successful Intercourse (SEP3)				
Endpoint	27.0%	41.3%	57.1%	57.0%
Change from baseline†	14.1%	27.8%	43.4%	44.2%
p-value*	-	0.0002	<0.0001	<0.0001

† Least-square estimate from ANCOVA model

* comparison to placebo for change from baseline

Results in the ED Population with Diabetes Mellitus

Stendra was evaluated in ED patients (n=390) with type 1 or type 2 diabetes mellitus in a randomized, double-blind, parallel, placebo-controlled fixed dose trial of 3 months in duration. The mean age was 58 years (range 30 to 78 years). The population was 80.5% White, 17.2% Black, 1.5% Asian, and 0.8% of other races. The mean duration of ED was approximately 6 years. In this trial, Stendra at doses of 100 mg and 200 mg demonstrated statistically significant improvement in all 3 primary efficacy variables as measured by the erectile function domain of the IIEF questionnaire; SEP2 and SEP3.

Mean Change From Baseline for Primary Efficacy Variables in ED Population with Diabetes Mellitus (from Stendra prescribing information)

	Placebo (N=127)	STENDRA 100 mg (N=126)	STENDRA 200 mg (N=126)
IIEF EF Domain Score			
Endpoint	13.2	15.8	17.3
Change from baseline†	1.8	4.5	5.4
p-value*	-	0.0017	<0.0001
Vaginal Penetration (SEP2)			
Endpoint	42.0%	54.0%	63.5%
Change from baseline†	7.5%	21.5%	25.9%
p-value*	-	0.0004	<0.0001
Successful Intercourse (SEP3)			
Endpoint	20.5%	34.4%	40.0%
Change from baseline†	13.6%	28.7%	34.0%
p-value*	-	<0.0001	<0.0001

† least-square estimate from ANCOVA model
* comparison to placebo for change from baseline

SAFETY

Stendra is contraindicated in patients using any form of organic nitrate (either regularly or intermittently) and those with hypersensitivity to any component of the Stendra tablet.

This drug is not indicated in women and is pregnancy category C. Stendra is not indicated for use in pediatric patients and safety and efficacy in patients below 18 years has not been established. It is not recommended for use in patients with severe renal or hepatic impairment.
Stendra has drug interactions with strong CYP3A4 inhibitors and concurrent use should be avoided. It may be used with moderate CYP3A4 inhibitors but at a reduced dose. If co-administered with an alpha-blocker, patients should be stable on the alpha blocker dose and start at the 50mg dose.
Like all of the other PDE-5 inhibitors Stendra carries warning for cardiovascular risk, priapism, sudden loss or change in vision, and sudden hearing loss.

Most common adverse reactions observed with Stendra (greater than or equal to 2%) include headache, flushing, nasal congestion, nasopharyngitis, and back pain.

DOSAGE

The recommended starting dose is 100mg. Stendra should be taken as needed approximately 30 minutes before sexual activity. The dose may be increased to a maximum dose of 200mg or decreased to 50mg depending on individual efficacy and tolerability. The lowest dose that provides benefit should be used. Sexual stimulation is required for response to treatment and the maximum recommended dosing frequency is once per day. Stendra can be taken with or without food.

If Stendra is used in patients taking a moderate CYP3A4 inhibitors the dose should not exceed 50mg in a 24-hour period. If a patient is stable on an alpha-blocker the recommended starting dose is 50mg.

COST

Drug	Cost per unit	Cost per QL (6 per 30 days)
Stendra (avanafil) 50, 100, 200mg tablet	AWP=$29	$174
Viagra (sildenafil citrate) 25, 50, 100mg tablet	AWP=$34	$204
Levitra (vardenafil) 2.5, 5, 10, 20mg tablet	AWP=$33.33	$200
Staxyn (vardenafil) 10mg oral distingrating tablet	AWP=$20.81	$125
Cialis (tadalafil) 2.5, 5, 10, 20mg tablet*	AWP=$38 (10&20 mg) AWP=$6.49 (5mg) AWP=$6.49 (2.5mg)	$39-228

*** = Cialis 2.5mg and 5mg is indicated for once-daily dosing; 5mg, 10mg, 20mg strengths are approved for as needed dosing**

FORMULARY PLACEMENT RECOMMENDATIONS

Based on this initial assessment of available clinical and financial information, consider NOT ADDING Stendra to the formulary pending complete review by the appropriate oversight committee for the plan.

REFERENCES

- Stendra [Prescribing Information]. Mountain View, CA: Vivus, Inc; October 2012.
- FDA News Release April 17th, 2012) FDA approved Stendra for erectile dysfunction. Retrieved January 15th, 2014 from http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm302140.htm
- Kedia, George T. Avanafil for the treatment of erectile dysfunction: initial data and clinical key properties. Therapeutic Advances in Urology. 2013 February; 5(1): 35–41.