



Therapeutic Class ReviewSM

Sildenafil (RevatioTM)

November 2005

New Product for Review:
sildenafil (RevatioTM) [Pfizer]

Dossier Provided by Manufacturer: No

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Preferred/Non-Formulary
bosentan (Tracleer [®]) [Actelion]	

Drugs covered under Medical Benefit	
epoprostenol (Flolan [®]) [#] [GlaxoSmithKline]	
treprostinil (Remodulin [®]) [#] [United Therapeutics]	
Iloprost (Ventavis [®]) ^{##} [CōTHERIX]	

[#] medication is a non-self administered, injectable product.

^{##} medication is non-self administered, inhaled product.

Executive Summary

- Revatio is a new oral medication approved for use in the treatment of PAH.
- It contains the same active ingredient (sildenafil) as Viagra[®], a medication used to treat erectile dysfunction.
- The tablet strengths and dosing regimens used for treating these two conditions are different.
- There is a potential for off-label use of Revatio in the treatment of erectile dysfunction.
- For treatment of PAH, there are very few treatment options available.
- The role of the new treatment options in the treatment of PAH is still emerging.

Evidence:

- There is no published evidence that supports the use of Revatio in the treatment of PAH.
- There is unpublished data from a single pivotal trial with Revatio that demonstrated improvement in exercise capacity (6-minute walk test) in patients with PAH that had NYHA class II and III symptoms.

- The baseline symptoms of the patients studied in the Revatio trial were less severe than those studied in trials with other PAH agents (based on NYHA class).
- There are no RCTs that compare Revatio with other currently established treatments for PAH.
- There is no good evidence that the safety of Revatio is superior to other agents used to treat PAH.
- There is no evidence that Revatio provides additional benefit when given concomitantly with other PAH treatments.

Conclusion

Sildenafil (Revatio™) is a preferred/formulary product because:

- it is an additional option in a condition with few treatment options,
- it offers another step before progressing to more invasive therapies, and
- it is available at a lower cost than other treatment options.

Products

Drug Product	Date of FDA Approval	FDA Approved Indications	Dose/Route	AWP Cost*	Potential Off-Label Uses
bosentan (Tracleer®) ^{1, 6}	11/2001	Treatment of pulmonary arterial hypertension (PAH) in patients with WHO class III or IV symptoms, to improve exercise ability and decrease the rate of clinical worsening.	125 mg orally twice daily	\$3885	congestive heart failure; hypertension
epoprostenol (Flolan®) ^{2, 6}	09/1995	(1) Long-term intravenous treatment of primary PAH and (2) pulmonary hypertension associated with scleroderma spectrum of disease in NYHA Class III and IV patients who do not respond adequately to conventional therapy.	<i>initial/titration:</i> 2 ng/kg/min via intravenous infusion, then increase every 15 minutes by 2 ng/kg/min until adverse effects. (dose highly variable; typically in 20 to 40ng/kg/min range)	\$2100 to \$4200 (based on dose of 20 to 40 ng/kg/min) [does not include cost of infusion or monitoring]	lung transplantation; cardiopulmonary bypass
iloprost (Ventavis®) ^{3, 6}	12/2004	Treatment of PAH (WHO group I) in patients with NYHA Class III or IV symptoms. (Ventavis has not been adequately studied with concomitant use of other approved therapies for PAH)	2.5 to 5 mcg via inhalation 6 to 9 times per day. <i>maximum:</i> 5mcg per dose; 45 mcg per day.	\$6605 to \$9907	concomitant treatment with other PAH agents; peripheral vascular disease; angina pectoris
sildenafil (Revatio™) ^{4, 6}	06/2005	Treatment of PAH (WHO Group I) to improve exercise ability.	20 mg orally three times daily.	\$1005	erectile dysfunction
treprostinil (Remodulin®) ^{5, 6}	05/2002	For the treatment of PAH in patients with NYHA Class II to IV symptoms to diminish symptoms associated with exercise.	1.25 ng/kg/min via subcutaneous or intravenous infusion. Increase in increments of 1.25 ng/kg/min per week; <i>maximum:</i> 40 ng/kg/min.	\$3932 to \$7865 (based on 20 to 40 ng/kg/min) [does not include cost of infusion or monitoring]	heart failure

*AWP (average wholesale price) based on First Data Bank as of August 2005 for 30 days of therapy.

WHO classification = World Health Organization classification of PAH (see *Appendix D* for group definitions)

NYHA classification= New York Heart Association functional classification by symptoms (see *Appendix D* for definitions)

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